ANTIDIABETIC MEDICATION PERSISTENCE AND IMPLEMENTATION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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INTRODUCTION

- Glycemic control contributes to both slowing chronic kidney disease (CKD) progression and reducing the risk of cardiovascular mortality and morbidity.
- Most diabetic patients have to use antidiabetic drugs (AD) to achieve gly-cemic control.
- Those drugs have to be taken every day during a long period of time.

AIMS

Among individuals suffering from CKD newly treated with an AD:

- To estimate persistence with AD 1 year after AD treatment initiation.
- Among those persisting, to estimate treatment implementation in the year following AD initiation.
- To identify factors associated with persistence.
- To identify factors associated with implementation.

METHODS

Study design and data sources

- We carried out a cohort study using Quebec administrative databases. Da-tabases provide information on patient's demographics (age, sex, socio-economic status), outpatient medical services, date of diagnosis, physi-cian specialty, use of drugs and hospitalizations.

Study population

- Inclusion criteria:
 - Individuals aged ≥ 18 years old newly diagnosed with CKD between 1 January 2000 and 31 December 2011.
 - Had a first claim for any AD at the time of CKD diagnosis or after.
- Exclusion criteria:
 - Individuals not eligible to the RAMQ drug plan 365 days before and 365 days after the date of AD treatment initiation.
 - Those who moved out from the province of Quebec.
 - Those who died on the date of their 1st CKD diagnosis or died during the hospital stay in which CKD was first diagnosed.

Variables

Outcome variables

- Persistence with AD**
 - If individuals had a provision of any AD at the 1st year anniversary date of treatment initiation according to most recent dispensing (+ permissible gap of 1.5 times the days' supply).
- Implementation of AD**
 - If individuals were persistent and had $\geq 80\%$ of days covered by any AD between CKD diagnosis and day 365.

Figure 1. Timeline measure of variable

Statistical analysis

- We identified factors associated with persistence and with implementa-tion using modified Poisson regression.
- Sensitivity analyses were conducted for persistence (permissible gaps of 1.0 and 1.5 time the days' supply) and implementation ($\geq 70\%$, ≥ 80 and $\geq 90\%$ of days covered).

RESULTS

- Among 6,671 individuals included in our study population, 5,128 (76.9%) were persistent.

Table 1. Adjusted prevalence ratios of patients' characteristics and persistence with antidiabetic drug treatment 365 days after treatment initiation (N = 6,671)

Characteristics	Persistent				Adjusted prevalence ratio	95% confidence interval	P-value
	Yes N = 5,128 (76.9%)		No N = 1,543 (23.1%)				
	N	%	N	%			
Age (years)							
18-63	1,018	19.8	299	19.4	1.00		
64-70	1,064	20.8	282	18.3	0.99	0.95-1.04	0.865
71-75	1,009	19.7	299	19.4	0.97	0.93-1.02	0.249
76-81	1,110	21.6	360	23.3	0.96	0.92-1.01	0.091
> 81	927	18.1	303	19.6	0.97	0.92-1.02	0.214
Sex							
Male	2,913	56.8	884	57.3	1.00		
Female	2,215	43.2	659	42.7	1.01	0.98-1.04	0.602
Socio-economic status							
High	2,115	41.3	695	45.1	1.00		
Medium	2,120	41.3	596	38.6	1.03	1.01-1.07	0.030
Low	893	17.4	252	16.3	1.04	0.99-1.08	0.093
Specialty of prescriber of initial AD treatment							
General practitioner	3,765	73.4	1,077	69.8	1.00		
Nephrologist	334	6.5	115	7.5	0.95	0.90-1.01	0.105
Internist	382	7.5	104	6.7	1.02	0.97-1.07	0.388
Other	641	12.5	245	15.9	0.94	0.90-0.98	0.007
Missing	6	0.1	2	0.1	NA		
No of physician visits in the year before AD treatment initiation							
0-10	1,775	34.6	422	27.4	1.00		
11-22	1,697	33.1	520	33.7	0.96	0.93-0.99	0.030
> 22	1,656	32.3	601	38.9	0.93	0.90-0.97	0.001
No of distinct drugs in the year before AD treatment initiation							
0-9	1,663	32.4	493	32.0	1.00		
10-15	1,851	36.1	485	31.4	1.03	0.99-1.06	0.085
> 15	1,814	31.5	565	36.6	0.98	0.94-1.02	0.321
Time from diagnosis of CKD up to initial AD treatment (days)							
0-11	1,006	19.6	331	21.5	1.00		
12-180	949	18.5	381	24.7	0.96	0.91-1.00	0.070
181-548	1,066	20.8	268	17.4	1.05	1.01-1.10	0.022
549-1,189	1,038	20.2	299	19.4	0.99	0.95-1.04	0.773
> 1,189	1,069	20.9	264	17.0	1.02	0.97-1.07	0.389
Initial AD treatment modalities							
Metformin mono-therapy	2,219	43.2	666	43.2	1.00		
Sulfonylureas monotherapy	1,295	25.3	421	27.3	1.00	0.97-1.03	0.852
Insulin monotherapy	428	8.4	165	10.7	0.98	0.93-1.03	0.413
Other monotherapy	436	8.5	139	9.0	1.01	0.96-1.06	0.759
Multiple therapy	750	14.6	152	9.8	1.12	1.08-1.16	<0.01
Hospitalization in the year before AD treatment initiation							
No	1,683	32.8	353	22.9	1.00		
Yes	3,445	67.2	1,190	77.1	0.88	0.84-0.91	<0.01
Hypertension							
No	1,709	33.3	493	31.9	1.00		
Yes	3,419	66.7	1,050	68.1	1.04	1.01-1.07	0.020
Dyslipidemia							
No	3,404	66.4	1,041	67.5	1.00		
Yes	1,724	33.6	502	32.5	1.06	1.03-1.10	<0.01
Stroke							
No	4,804	93.7	1,458	94.5	1.00		
Yes	324	6.3	85	5.5	1.05	1.01-1.11	0.045
Coronary disease							
No	2,129	41.5	644	41.7	1.00		
Yes	2,999	58.5	899	58.3	1.03	1.01-1.06	0.030
Anemia							
No	4,786	93.3	1,413	91.6	1.00		
Yes	342	6.7	130	8.4	0.98	0.92-1.04	0.446

Table 2. Adjusted prevalence ratios of patients' characteristics and implementation of antidiabetic drug treatment among those persisting with their antidiabetic treatment 365 days after treatment initiation (N = 5,128)

Characteristics	Adequate implementation				Adjusted prevalence ratio	95% confidence interval	P-value
	Yes N = 4,506 (87.9%)		No N = 622 (12.1%)				
	N	%	N	%			
Age (years)							
18-63	875	19.4	143	23.0	1.00		
64-70	933	20.7	131	21.1	1.03	0.99-1.06	0.083
71-75	868	19.3	141	22.7	1.01	0.97-1.05	0.617
76-81	983	21.8	127	20.4	1.03	0.99-1.07	0.095
> 81	847	18.8	80	12.8	1.06	1.02-1.10	0.002
Sex							
Male	2,518	55.9	395	63.5	1.00		
Female	1,988	44.1	227	36.5	1.02	1.01-1.04	0.048
Socio-economic status							
High	1,827	40.5	288	46.3	1.00		
Medium	1,882	41.8	238	38.3	1.01	0.98-1.03	0.463
Low	797	17.7	96	15.4	1.04	1.01-1.07	0.029
Specialty of prescriber of initial AD treatment							
General practitioner	3,339	74.1	426	68.5	1.00		
Nephrologist	283	6.3	51	8.2	0.97	0.92-1.01	0.156
Internist	333	7.4	49	7.9	0.98	0.94-1.02	0.335
Other	548	12.1	93	14.9	0.96	0.93-0.99	0.046
Missing	3	0.1	3	0.5	NA		
No of physician visits in the year before AD treatment initiation							
0-10	1,532	34.0	243	39.1	1.00		
11-22	1,528	33.9	169	27.2	1.03	1.01-1.06	0.020
> 22	1,446	32.1	210	33.7	0.99	0.96-1.02	0.675
No of distinct drugs in the year before AD treatment initiation							
0-9	1,409	31.3	254	40.8	1.00		
10-15	1,651	36.6	200	32.2	1.05	1.02-1.07	0.001
> 15	1,446	32.1	168	27.0	1.05	1.02-1.08	0.001
Time from diagnosis of CKD up to initial AD treatment (days)							
0-11	891	19.8	115	18.5	1.00		
12-180	838	18.6	111	17.9	0.99	0.97-1.03	0.982
181-548	935	20.8	131	21.1	0.98	0.96-1.02	0.515
549-1,189	899	19.9	139	22.3	0.99	0.96-1.03	0.575
> 1,189	943	20.9	126	20.2	1.01	0.98-1.05	0.418
Initial AD treatment modalities							
Metformin mono-therapy	1,939	43.0	280	45.0	1.00		
Sulfonylureas monotherapy	1,130	25.1	165	26.5	0.99	0.97-1.02	0.798
Insulin monotherapy	366	8.1	62	10.0	0.98	0.95-1.03	0.592
Other monotherapy	375	8.3	61	9.8	0.98	0.94-1.02	0.420
Multiple therapy	696	15.5	54	8.7	1.06	1.03-1.09	<0.01
Hospitalization in the year before AD treatment initiation							
No	1,449	32.2	234	37.6	1.00		
Yes	3,057	67.8	388	62.4	1.01	0.97-1.04	0.855
Hypertension							
No	1,485	33.0	224	36.0	1.00		
Yes	3,021	67.0	398	74.0	1.01	0.98-1.03	0.901
Dyslipidemia							
No	2,967	65.9	437	70.3	1.00		
Yes	1,539	34.1	185	29.7	1.02	0.99-1.04	0.163
Stroke							
No	4,216	93.6	588	94.5	1.00		
Yes	290	6.4	34	5.5	1.02	0.98-1.06	0.465
Coronary disease							
No	1,851	41.1	278	44.7	1.00		
Yes	2,655	58.9	344	55.3	1.01	0.98-1.03	0.797
Anemia							
No	4,198	93.2	588	94.5	1.00		
Yes	308	6.8	34	5.5	1.01	0.97-1.05	0.612

DISCUSSION

- Overall, 32% of patients with CKD who initiated an AD may not fully bene-fit from it as they were either non-persistent or had inadequate treatment implementation.
- 11 characteristics were associated with persistence and 8 with implementa-tion. Only 3 were associated with both (another specialist as prescriber of the first AD claim, between 11 and 22 physician visits in the year before AD treatment initiation, and a multiple therapy at treatment initiation). This confirms that persistence and implementation are two different con-structs of adherence.
- However, observed associations were weak in magnitude.

Strengths

- Large sample size, new-user design, population-based for those aged ≥ 65 years.
- Real-life practice setting.
- Assessment of both persistence and implementation, two different con-structs of adherence.

Limitations

- Drugs claimed were assumed to be taken.
- Lack of information on psychosocial variables (e.g. patient's perception of risk of disease and benefits of the treatment) that are likely to influence drug persistence and implementation.

CONCLUSION

Results could help target individuals who need help to bet-ter manage their AD treatment.

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