DATA MATTERS

Adherence to Prescribing Recommendations Made on a Provincial Formulary

Suivi des recommandations pour les médicaments d'ordonnance indiquées sur un formulaire provincial

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Abstract

Guidance regarding appropriate and cost-effective use of prescription drugs is published in the Ontario Drug Benefit Formulary in the form of "therapeutic notes." We conducted a cross-sectional study of all residents of Ontario aged 66 and older who received a new prescription for one of two drugs, aliskiren or sitagliptin, between December 1, 2008 and March 31, 2012 to determine how frequently such guidance is followed. Approximately half of initial prescriptions for aliskiren and sitagliptin were prescribed in a manner that did not conform to the therapeutic note recommendations (51.4% and 49.3%, respectively). Given this high rate of non-conformance, policy makers may wish to use other mechanisms to influence prescriber behaviour to improve the quality and efficiency of healthcare.

Résumé

Les recommandations visant une utilisation adéquate et efficace par rapport au coût des médicaments sur ordonnance sont publiées dans le Formulaire des médicaments de l'Ontario sous la forme de « notes thérapeutiques ». Nous avons effectué une étude transversale de tous les résidents de l'Ontario âgés de 66 ans et plus qui ont reçu une nouvelle ordonnance pour un des deux médicaments, aliskirène ou sitagliptine, entre le 1er décembre 2008 et le 31 mars 2012 afin de déterminer à quel point les recommandations sont suivies. Environ la moitié des premières ordonnances pour l'aliskirène et la sitagliptine ont été prescrites d'une façon qui ne respecte pas les recommandations des notes thérapeutiques (51,4 % et 49,3 %, respectivement). Étant donné ce taux élevé de non-conformité, les responsables de politiques pourraient souhaiter employer d'autres mécanismes visant à influencer le comportement des prescripteurs afin d'améliorer la qualité et l'efficience des services de santé.

The optimal allocation of resources in healthcare requires that interventions be delivered judiciously (Birch et al. 1993; Mitton and Donaldson 2002). A variety of mechanisms exist to ensure that interventions are broadly available when proven efficacious and cost-effective, and restricted when not cost-effective (McMahon et al. 2006; Morgan et al. 2006). With respect to prescription drugs, the bluntest instruments are simply to deny public reimbursement or deny regulatory approval. These mechanisms are typically used when there are major safety concerns or a lack of evidence supporting efficacy, and sometimes also when a drug is extraordinarily expensive (McMahon et al. 2006). However, many medications are effective or cost-effective for some patients but not for others. In addition to subtler methods used to guide prescribing, such as clinical practice guidelines, decision support tools and educational outreach, the implementation of moderately stringent reimbursement restriction mechanisms has shown to be effective in these cases

(Marshall et al. 2006; Wettermark et al. 2010). The use of less stringent prescribing guidance embedded within a formulary has not been studied, yet is commonly used in Ontario, Canada (Laupacis 2002).

This form of guidance, referred to as "therapeutic notes" in Ontario, is published in the Ontario Drug Benefit Formulary and is primarily intended to promote cost-effective prescribing. Physicians are encouraged, but not required, to follow the guidelines provided in the therapeutic notes (MOHLTC 2013), and anecdotal evidence suggests that many medications are used in a manner that is inconsistent with these recommendations. The objective of our study was to determine how frequently such guidance is followed and to determine patient and prescriber characteristics that are associated with non-conformance – i.e., prescribing that is not in accordance with the therapeutic note recommendations.

Materials and Methods

We conducted a retrospective cross-sectional study using several linked healthcare databases in Ontario. In 2013, the province had a population of nearly 13 million residents who had universal access to hospital and physician services (Statistics Canada 2013). Almost 2 million of these residents were aged 65 years or older and received universal drug coverage that could be captured in administrative databases. Although there were approximately 200 drug products listed with therapeutic notes on the Ontario Drug Benefit Formulary at the time of this study, most simply provided information about dosing, side effects or interactions. Of those that specified a drug should be used only in specific clinical circumstances, many had clinical criteria that did not lend themselves to examination using administrative data. We selected aliskiren and sitagliptin for this study because they were the only drug products in which the therapeutic notes were stable over time and specified clinical criteria that could be operationalized using our administrative data sources. We conducted this study according to a pre-specified protocol and obtained ethics approval from the Research Ethics Board at Sunnybrook Health Sciences Centre (Toronto, Ontario).

We ascertained patient characteristics, prescriber characteristics, prescription drug use and outcome data from the records of five databases linked through the Institute of Clinical Evaluative Sciences (ICES). These include the Registered Persons Database (RPDB), which records vital status and patient demographics; the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD), which records diagnostic and procedural information during hospital admissions; and the Ontario Health Insurance Plan (OHIP) database, which contains health claims for both in-patient and outpatient physician services. We used the Ontario Drug Benefit (ODB) database to identify prescription drug use and the ICES Physician Database (IPDB) to obtain prescriber information. The ODB database contains highly accurate records of all outpatient prescriptions dispensed to patients aged 65 years or older (Levy et al. 2003).

We established two separate cohorts of residents of Ontario aged 66 and older who filled a new outpatient prescription for aliskiren or sitagliptin between December 1, 2008 and March 31, 2012 and analyzed them separately (sitagliptin was available on formulary only from June 1, 2010). We excluded the following patients from the analysis: (a) those who received a prescription for the study drug in the year prior to cohort entry to ensure that patients included in the study were new users, (b) those in their first year of eligibility for prescription drug coverage (aged 65 years) to avoid incomplete medication records and (c) those with missing prescriber information in IPDB (this accounted for 2,243 [8.8%] records in the aliskiren cohort and 4,602 [9.6%] records in the sitagliptin cohort). We then established separate cohorts of all unique physicians who wrote the initial prescription for aliskiren or sitagliptin to patients in each respective patient cohort.

The prescribing recommendations listed on the Ontario Drug Benefit Formulary for aliskiren and sitagliptin are reported in Box 1. The maximum drug coverage for prescriptions under the Ontario Drug Benefit program is 100 days' duration. We defined non-conformance in the aliskiren cohort as the absence of a prescription for both a thiazide diuretic and either an angiotensin converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) during the 120 days prior to the aliskiren prescription. For the sitagliptin cohort, we defined non-conformance as the absence of a prescription for metformin at the maximum dose of 2,000 mg/day during the 120 days prior to the sitagliptin prescription. We were unable to ascertain information on blood pressure control, glycaemic control or drug intolerance.

BOX 1. Therapeutic notes listed on the Ontario Drug Benefit Formulary

Aliskiren

"For patients with moderate hypertension who have not achieved blood pressure targets while on maximally optimized therapy with a thiazide-diuretic and an angiotensin converting enzyme inhibitor (ACEi) OR a thiazide-diuretic and an angiotensin II receptor blocker (ARB)." (MOHLTC 2009)

Sitagliptin

"For treatment of Type 2 diabetes in patients on maximal doses of metformin (2,000 mg/day) who have:

1. *Inadequate glycemic control (defined as HbA1c >0.07) and intolerance or contraindication to a sulfonylurea; or*
2. *A HbA1c less than or equal to 0.07 and elevated 2 hour post prandial glucose (PPG >10 mmol/L) or fasting plasma glucose (FPG >7 mmol/L) levels and intolerance or contraindication to a sulfonylurea; or*
3. *Inadequate glycemic control (HbA1c >0.07) and on maximal doses of a sulfonylurea and for whom insulin is not an option" (MOHLTC 2010)*

We analyzed data acquired from the aliskiren and sitagliptin cohorts separately. In each cohort, we used descriptive statistics to summarize patient and prescriber characteristics and determine the proportion of patients that received non-conforming prescriptions. As an exploratory analysis, we used simple logistic regression and multivariable logistic regression, adjusting for potential confounders (remaining predictor variables included in the model), to determine patient and prescriber characteristics associated with non-conformance to therapeutic notes. We used a generalized estimating equation in both cases to account for potential clustering of patient data by physician. We conducted all analyses with SAS, version 9.2 (SAS Institute Inc, Cary, NC).

Results

Among Ontarians aged 66 and older, there were 23,291 patients who received a new prescription for aliskiren and 43,196 patients who received a new prescription for sitagliptin during the study period. Characteristics of these patients are outlined in Table 1. Overall, 11,967 (51.4%) patients received prescriptions for aliskiren that did not conform to the therapeutic notes criteria; 21,308 (49.3%) patients received prescriptions for sitagliptin that did not conform to the therapeutic notes criteria.

There were 3,608 physicians who initiated patients on aliskiren and 6,421 physicians who initiated patients on sitagliptin during our study period. Among these physicians, the majority were male and approximately 80% were general practitioners or family physicians. The median number of patients initiated on aliskiren or sitagliptin per physician during the 3.3-year accrual period was two (range, 1–56) for aliskiren and three (range, 1–46) for sitagliptin. Results of the adjusted models to evaluate prescriber characteristics associated with the receipt of non-conforming prescriptions in both cohorts are reported in Tables 2 and 3. After adjustment for potential confounders, none of the observed prescriber characteristics was strongly associated with non-conformance.

TABLE 1. Characteristics of all new older users of aliskiren and sitagliptin in Ontario, Canada

Patient characteristics	Aliskiren cohort (n=23,291)	Sitagliptin cohort (n=43,196)
Demographics and health status		
Age, median (IQR)	75.1 (70.4–80.6)	73.4 (69.3–78.7)
Sex (female)	13,321 (57.2%)	20,531 (47.5%)
Income quintile		
Lowest income quintile	5,195 (22.3%)	9,334 (21.6%)
Second income quintile	5,258 (22.6%)	9,789 (22.7%)
Third income quintile	4,693 (20.2%)	8,793 (20.4%)
Fourth income quintile	4,367 (18.8%)	8,094 (18.7%)
Highest income quintile	3,710 (15.9%)	7,041 (16.3%)
Rural residence	2,123 (9.1%)	4,198 (9.7%)
Residence in a long-term care facility	483 (2.1%)	1,107 (2.6%)
Charlson co-morbidity index		
0	2,292 (9.8%)	1,204 (2.8%)
1	1,614 (6.9%)	3,183 (7.4%)
≥ 2	2,997 (12.9%)	7,396 (17.1%)
No hospitalization	16,388 (70.4%)	31,413 (72.7%)
Diabetes mellitus	8,974 (38.5%)	43,196 (100.0%)
Chronic kidney disease	2,569 (11.0%)	2,658 (6.2%)
End-stage renal disease	259 (1.1%)	–
Alcoholism	–	53 (0.12%)
Chronic liver disease	–	512 (1.2%)
Congestive heart failure	–	2,473 (5.7%)

"–" indicates that this variable was not assessed in the cohort specified.

TABLE 2. Patient and prescriber characteristics associated with the receipt of aliskiren prescriptions that do not conform to the therapeutic notes criteria

Risk factor	Unadjusted odds ratio (95% CI) (primary outcome)	Adjusted odds ratio (95% CI) (primary outcome)
Patient characteristic		
Increased age	1.01 (1.01 to 1.02)	1.01 (1.00 to 1.01)
Sex (female)	0.89 (0.85 to 0.94)	0.86 (0.81 to 0.91)
Rural residence	0.97 (0.88 to 1.07)	0.94 (0.83 to 1.08)
Residence in a long-term care facility	1.67 (1.36 to 2.05)	1.49 (1.19 to 1.89)
Diabetes mellitus	0.71 (0.67 to 0.75)	1.10 (0.92 to 1.30)
Chronic kidney disease	1.38 (1.24 to 1.52)	1.19 (1.04 to 1.37)
End-stage renal disease	2.22 (1.70 to 2.91)	1.52 (1.11 to 2.08)
Increased number of distinct drugs dispensed	0.98 (0.98 to 0.99)	0.96 (0.95 to 0.97)
Increased number of outpatient physician visits in last year	1.00 (1.00 to 1.01)	1.01 (1.01 to 1.01)
In-patient hospital admission in last year	1.33 (1.24 to 1.43)	0.95 (0.86 to 1.05)
Visit to outpatient endocrinologist in last year	0.82 (0.74 to 0.91)	0.93 (0.83 to 1.05)
Visit to outpatient nephrologist in last year	1.18 (1.06 to 1.32)	0.96 (0.83 to 1.11)
Visit to outpatient cardiologist in last year	1.06 (1.00 to 1.13)	1.02 (0.94 to 1.10)
Prescriber characteristic		
Sex (female)	0.99 (0.90 to 1.08)	1.08 (0.97 to 1.19)
Increased years of practice	1.00 (1.00 to 1.01)	1.00 (1.00 to 1.01)
Rural practice	1.00 (0.86 to 1.17)	1.01 (0.83 to 1.22)
Canadian medical graduate	0.97 (0.90 to 1.06)	0.97 (0.89 to 1.06)
Subspecialty		
Nephrologist	1.28 (1.10 to 1.49)	1.19 (0.98 to 1.43)
Endocrinologist	0.54 (0.41 to 0.72)	0.73 (0.53 to 1.01)
Cardiologist	0.84 (0.73 to 0.98)	0.83 (0.71 to 0.97)
Other specialist	1.03 (0.88 to 1.20)	1.03 (0.88 to 1.20)

Other variables included in the model: Charlson co-morbidity index, prescriptions for select drugs in last 120 days (beta-blocker, calcium channel blocker, loop diuretic, potassium-sparing diuretic, alpha-blocker, vasodilator, alpha-adrenergic agonist, acetylsalicylic acid, clopidogrel, digoxin, statin, oral antihyperglycaemic, insulin).

TABLE 3. Patient and prescriber characteristics associated with the receipt of sitagliptin prescriptions that do not conform to the therapeutic notes criteria

Risk factor	Unadjusted odds ratio (95% CI) (primary outcome)	Adjusted odds ratio (95% CI) (primary outcome)
Patient characteristic		
Increased age	1.03 (1.03 to 1.03)	1.03 (1.03 to 1.04)
Sex (female)	1.20 (1.16 to 1.24)	1.22 (1.18 to 1.27)
Rural residence	1.01 (0.94 to 1.08)	1.00 (0.91 to 1.09)
Residence in a long-term care facility	1.49 (1.31 to 1.69)	1.12 (0.96 to 1.30)
Chronic kidney disease	2.16 (1.98 to 2.37)	1.77 (1.56 to 2.01)
Alcoholism	1.29 (0.77 to 2.15)	1.12 (0.63 to 1.97)
Chronic liver disease	1.33 (1.12 to 1.59)	1.23 (1.02 to 1.48)
Congestive heart failure	1.44 (1.32 to 1.56)	1.25 (1.14 to 1.38)
Increased number of distinct drugs dispensed	0.98 (0.98 to 0.98)	0.99 (0.98 to 0.99)
Increased number of outpatient physician visits in last year	1.00 (1.00 to 1.00)	1.00 (1.00 to 1.01)
In-patient hospital admission in last year	1.30 (1.22 to 1.38)	1.02 (0.94 to 1.10)
Visit to outpatient endocrinologist in last year	0.80 (0.74 to 0.85)	0.88 (0.81 to 0.96)
Visit to outpatient nephrologist in last year	1.97 (1.80 to 2.15)	1.60 (1.41 to 1.81)
Visit to outpatient internal medicine specialist in last year	1.06 (1.00 to 1.12)	1.06 (0.99 to 1.14)
Prescriber characteristic		
Sex (female)	0.95 (0.90 to 1.01)	0.95 (0.89 to 1.01)
Increased years of practice	1.00 (1.00 to 1.00)	1.00 (1.00 to 1.00)
Rural practice	1.05 (0.95 to 1.15)	1.06 (0.94 to 1.20)
Canadian medical graduate	1.00 (0.94 to 1.05)	0.97 (0.92 to 1.03)
Subspecialty		
Nephrologist	1.66 (1.25 to 2.20)	0.98 (0.72 to 1.33)
Endocrinologist	0.75 (0.67 to 0.83)	0.96 (0.84 to 1.09)
Internal medicine specialist	0.86 (0.75 to 0.99)	0.88 (0.76 to 1.01)
Other specialist	1.06 (0.93 to 1.21)	1.03 (0.89 to 1.19)

Other variables included in the model: Charlson co-morbidity index, prescriptions for select drugs in last 120 days (sulfonylurea, insulin, alpha-glucosidase inhibitor, meglitinide, thiazolidinedione, acetylsalicylic acid, clopidogrel, statin).

Discussion

In this study of all older patients in Ontario initiating aliskiren and sitagliptin between December 1, 2008 and March 31, 2012, we found that approximately half of patients started on one of the two drugs did not meet the appropriateness criteria in the formulary, and less than one-quarter of physicians consistently followed these recommendations. These results suggest that therapeutic notes have a limited impact on physician prescribing behaviour and are in keeping with previous literature confirming that interventions relying solely on passive dissemination of information are generally ineffective (Grimshaw et al. 2001; Grindrod et al. 2006). The implication is that therapeutic notes should not be relied upon to promote safe or cost-effective prescribing.

There are several possible explanations for the lack of effectiveness of therapeutic notes demonstrated. These include vague or poorly written recommendations, lack of physician awareness of the presence of these recommendations on the provincial formulary, or absence of a requirement to attain approval for use of the drug according to the recommended clinical criteria. In cases where the desired outcome is that medications be prescribed only to patients who meet particular clinical criteria, other mechanisms such as prior authorization programs or reimbursement restriction would be more effective (Fischer et al. 2004; Grindrod et al. 2006; Wettermark et al. 2010). However, in cases where therapeutic notes simply serve to inform physicians of cost-effective and evidence-based prescribing, implementation of multifaceted interventions using computerized clinical decision support systems, prescriber feedback or educational outreach programs (also known as academic detailing) in conjunction with therapeutic notes may be more likely to improve compliance (Avorn and Soumerai 1983; Garg et al. 2005; Grimshaw et al. 2001; Grindrod et al. 2006; Hux et al. 1999; Solomon 2001). As primary care providers are initiating these drugs in over 80% of cases, interventions to modify prescribing behaviour should be specifically targeted at this group.

Given the complexity of clinical conditions and rapidly growing evidence base, physicians could conceivably rationalize use of these drugs outside of the therapeutic note recommendations based on clinical circumstances not accounted for by the notes or in response to new evidence, regardless of the strategy used to enforce them. The patient characteristics associated with the receipt of non-conforming prescriptions identified for aliskiren or sitagliptin, such as the presence of chronic kidney disease, highlight the importance of the clinical scenario. Preliminary data from the ALTITUDE (Aliskiren Trial in Type 2 Diabetes Using Cardio-Renal Endpoints) study indicating increased risk of adverse events (hypotension, hyperkalemia, non-fatal stroke) and lack of benefit among patients with type 2 diabetes and chronic kidney disease on dual renin-angiotensin system (RAS) blockade with aliskiren may have been responsible for non-conforming prescribing in the aliskiren cohort prior to its removal from the Ontario Drug Benefit Formulary in December 2012 (Novartis 2011; Ontario Public Drug Programs 2012; Parving et al. 2008). However, these new data likely had only a very small impact on our study given that the preliminary results of the trial became publicly known just three months before the end of our study period.

We were not able to identify any prescriber characteristics that were independently associated with non-conformance. While it is possible that these associations do not exist or are only weak, it is also possible that the lack of statistical significance is a result of the high degree of correlation among the predictor variables selected to include in the model, over-adjustment or insufficient statistical power. For this reason, these results should be viewed as exploratory in nature. The main limitation of our study is that we assessed only two drugs. It is possible that rates of non-conformance would be different for other medications. Another limitation of our study is that we relied on administrative data to assess drug prescribing and the use of health services. As we were not able to capture all components of the therapeutic note written in the Ontario Drug Benefit Formulary (such as blood pressure control, glycaemic control and medication intolerance), the true prevalence of non-conformance is almost certainly higher than we report.

Conclusion

Many publicly funded medications in Ontario are prescribed in a manner that is inconsistent with guidance published in the formulary. Policy makers should consider other mechanisms to promote cost-effective prescribing.

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