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Dr. Stephen Choi and Dr. Anita Palepu
Co-Editors
Open Medicine

Dear Dr. Choi and Dr. Palepu:

We are pleased to submit the enclosed article, "Factors related to splitting statin tablets: a population-based analysis in British Columbia" for publication in *Open Medicine*. The manuscript is not published or under review elsewhere, and all persons listed as authors have contributed sufficiently to the project to be included as authors. The manuscript contains 2399 words, 4 tables and 1 figure.

Tablet splitting is one way for patients to save on their prescription drug costs, yet little is known about how often splitting is done, and what characteristics of patients, physicians and pharmacies are associated with its use. Our analysis estimated the frequency of splitting statin tablets, and factors related to splitting in the only North American jurisdiction where comprehensive population data were available. The frequency of tablet splitting in British Columbia was low but increasing in frequency in the past 11 years; and it varied between different patient, physician and insurance characteristics. The low and increasing frequency of splitting provides a unique opportunity for both targeted educational efforts and drug plan incentives to increase this simple cost saving measure.

We look forward to your review.

Sincerely,

A handwritten signature in blue ink, appearing to read 'Colin Dormuth'.

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FACTORS RELATED TO SPLITTING STATIN TABLETS: A POPULATION-BASED ANALYSIS IN BRITISH COLUMBIA

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Running Title: Physician and patient characteristics of tablet splitters

2,399 words, 4 tables, 1 figure

ABSTRACT

Introduction: The price per mg for most statin medications decrease at higher strengths, and this provides an economic incentive to split tablets. Little is known about patient and physician factors related to splitting.

Objective: We sought to determine the frequency of splitting statins; and to evaluate patient, physician and insurance characteristics related to splitting.

Methods: Prescription claims for statins were obtained from the BC Ministry of Health. We used the ratio of tablets to days-supply in each prescription to estimate the frequency of splitting each statin. We used multivariable logistic regression to assess physician, patient and public insurance factors associated with splitting. We used cost and dispensed days supply information reported by pharmacies to estimate cost savings from splitting.

Results: During an 11-year study period, 2.6% of 7.2 million statin prescriptions were split. Lovastatin was the only scored statin and was the most likely to be split, followed by rosuvastatin and atorvastatin. Fifty percent of split prescriptions were prescribed by 6% of statin prescribers. Specialists were less likely to split statins than general practitioners (OR=0.43, 95% CI:0.40 to 0.46), and statins prescriptions that were fully covered by the public drug plan were half as likely to be split than ones with no public coverage (OR=0.48, 95% CI: 0.44 to

0.92). British Columbians saved \$2.3 million splitting statins in 2006.

Conclusions: The frequency of tablet splitting in British Columbia was low but it increased over time. Splitting frequency varied between different insurance, patient and physician characteristics. The low frequency of splitting provides a unique opportunity for educational efforts and drug plan incentives to increase this simple cost saving measure.

Abstract word count: 268

Keywords: tablet splitting, statins, health policy

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Competing Interests: None

Contributions:

Colin Dormuth contributed methodological input, performed data analysis and drafted the manuscript

Sebastian Schneeweiss, Alan Brookhart, Ken Bassett, Greg Carney and Jim Wright all contributed methodological input and revised the manuscript

Stephen Adams contributed data analysis and revised the manuscript

INTRODUCTION

For many prescription drugs, the price per milligram declines substantially at higher strengths. This circumstance provides a compelling opportunity to substantially reduce costs by splitting tablets, often to obtain the same dose at half the price. In the United States, some major drug plan providers have implemented tablet splitting programs targeting statins (^{1,2}). Tablet splitting has been shown to substantially reduce prescription costs (Error: Reference source not found,^{3,4}) without negatively affecting laboratory outcomes or compliance (Error: Reference source not found,^{5,6,7}). In addition, patients have found tablet splitting to be simple and acceptable (Error: Reference source not found,⁸).

Little is known about patient and physician factors associated with splitting, or how common the practice is in Canada. When looking at aggregated 2005 data from British Columbia (BC), we noticed that the

average number of tablets per prescription varied among the statins. Since statins are only used for long-term prevention of heart attacks and stroke we thought that the most likely reason for the different average sizes of prescriptions was that some patients were splitting tablets. We looked for the most specific method to measure tablet splitting and used that to examine the frequency and predictors of splitting in a BC. Public and private insurers in BC have no programs that require or encourage splitting, meaning that the initiative for splitting comes solely from patients, pharmacists and physicians.

METHODS

Data

Prescription records were obtained from the PharmaNet database, which contains all prescriptions dispensed at community pharmacies in BC ⁽⁹⁾. We expect that underreporting and misclassification are very low because the PharmaNet system performs data quality checks. The PharmaNet data available to us did not include prescriptions for federally insured patients (Status Indians, prisoners, RCMP and Canadian Forces). Together these groups composed about 4% of the population. Prescriptions were linked to Ministry of Health databases for medical services registration and premium subsidy income level. The completeness of similar databases in other North American

jurisdictions has been studied (^{10, 11, 12, 13, 14}), but we are unaware of any such analyses in British Columbia.

Prescription Drug Coverage in British Columbia

Residents ≥ 65 years of age had full public coverage for prescription ingredient costs prior to January 2002. Residents under 65 years of age were covered under a public plan that included a deductible and a coinsurance component. Between January 2002 and April 2003 patients over 65 paid a new charge of \$25 per prescription (\$10 for low-income patients). Coverage for families of all ages was combined into a single policy on May 1, 2003. The new policy included an income-based deductible and a 25% or 30% coinsurance payment. Full public coverage for patients in nursing facilities or on social income assistance was continued.

Population

With some exceptions, the source population included all people who were residents of BC at any time between January 1, 1996 and December 31, 2006 (the study period). The source population excluded federally insured patients because we lacked those data, patients receiving social income assistance because policy changes made that population unstable for analysis, and nursing home residents because their medication use was expected to be highly regulated. The source

population numbered 4.1 million in 2006 ⁽¹⁵⁾. The study population included all patients from the source population who received a statin from a community pharmacy.

Quantification of Statin Splitting

Each PharmaNet record included the number of tablets and days-supply of medication dispensed. We used the ratio of these two quantities to estimate tablets per day. We calculated relative frequencies for tablets-to-days-supply ratios, in ratio intervals that were 0.1 in width. For example, a prescription with a tablets-to-days-supply ratio of 0.26 would be counted in the ≥ 0.2 and < 0.3 ratio interval. Prescriptions with ratios exactly equal to 0.5 were presumed to have been split. Prescriptions with ratios exactly equal to 1.0 were presumed not split.

Factors Associated with Statin Splitting

We assessed factors associated with splitting in new users of statins. One benefit of studying first-time prescriptions to new users was that within-patient clustering was not a factor. Patients that received a statin were defined as new users if they had not received another statin for a period of at least two years beforehand. We compared new users who were presumed splitters (ratio=0.5) to those who were presumed non-splitters (ratio=1.0). New users who received

prescriptions with tablet-to-days-supply ratios other than 0.5 or 1.0 were excluded from the analysis to maximize the specificity of the outcome.

Potential factors associated with splitting were compared using logistic regression that used generalized estimating equations (GEE) to adjust standard errors for correlations between repeated observations on the same prescribers ⁽¹⁶⁾. Hence, the new users analysis was implicitly adjusted for clustering at the patient level by analyzing each patient only once, and explicitly at the physician level using the GEE method. The GEEs assumed an exchangeable correlation matrix. Odds ratios and corresponding 95% confidence intervals were estimated using the Genmod procedure in SAS, Version 9.1 (SAS Institute, Inc., Cary, North Carolina). Variables included were patient age, sex, household annual income (*high* > Can \$28,000, *moderate* > \$20,000 and ≤ \$28,000, and *low* < \$20,000) ⁽¹⁷⁾, public coverage for the prescription (full, partial, none), prescriber specialty (specialist or general practitioner), an indicator for whether the prescriber's last statin prescription was split, type of statin, an indicator variable for whether the smallest strength was dispensed, number of weeks dispensed, and pharmacy type (independent, chain or other). In a secondary analysis, we performed the same logistic regression on all statin patients (new plus continuing users) using the same variables. In that analysis, we used GEEs to

adjust standard errors for correlations between repeated observations on the same patients. Our computers were unable to simultaneously adjust for clustering within patients and physicians because the dataset was too large.

We estimated the cost-savings and potential cost savings from splitting in British Columbia in 2006. In this analysis, we subtracted one half of the mean cost per days-supply dispensed for non-split prescriptions of double the strength (e.g. 20mg of atorvastatin) from the mean cost per days-supply actually dispensed of the lower strength (e.g. atorvastatin 10mg). We estimated cost savings by multiplying that difference by the number of days-supply dispensed during the year. For an estimate of actual savings, we used the number of days supply dispensed in the 2.6 percent of prescriptions that we assumed had been split. We used 20% of the eligible days supply dispensed to estimate the potential savings that from splitting 20% of prescriptions. For an estimate of potential savings from splitting 100% of prescriptions, the theoretical maximum savings, we used 100% of the eligible days supply dispensed. All prescriptions with a tablet to days supply ratio of 0.5 or 1.0 were eligible for the analysis, with the exception of prescriptions for the largest strength of a statin because no larger tablet was available to be split. No adjustment was made for drug waste, the cost of tablet splitters, or additional work by pharmacists.

RESULTS

There were 7.2 million statin prescriptions dispensed during the 11-year study period. We estimated that 2.6% of those prescriptions were split (Table 1) and that there was an increasing trend in splitting over the period (Figure 1). In the last year of the analysis, rosuvastatin and atorvastatin were the most likely statins to be split (8% and 5% of prescriptions, respectively). Pravastatin (1.4%) and fluvastatin (a capsule, 0.5%) were the least likely to be split. Lovastatin, the only statin available in scored tablets, was split at a fairly constant rate of 2.5% to 3%. Fifty percent of split prescriptions were prescribed by only 6% of routine statin prescribers (more than 10 statin prescriptions written). Patient age, sex, income level, public insurance level and the choice of statin type were very similar between the 6% of frequent splitters and the others. However, the 6% of frequent splitters wrote 5 times as many statin prescriptions as the other 94%.

There were 312,760 statin prescriptions dispensed to new users. Those patients had a mean age of 62.9 years, 45% were women, 22% had low incomes, and 4% had moderate incomes (Table 2). Similar fractions of splitting and non-splitting patients were dispensed prescriptions that received partial public drug coverage. However, the fraction of patients that received full public coverage was lower for splitters than non-splitters (14% versus 25%), and the fraction that did not receive any

public coverage was greater (61% versus 50%).

Results of the multivariable logistic regression analysis are shown in Table 3. In new statin users, likelihood of splitting increased significantly with age until 65 before decreasing significantly. Female patients were 23% more likely to split than males ($p < 0.001$).

Prescriptions to low income patients were split 51% more than ones to higher income patients ($p < 0.001$). Splitting was less likely to happen if prescriptions were covered by public insurance, with partially covered claims 29% less likely to be split than non-covered ones ($p < 0.001$), and fully covered prescriptions were 52% less likely to be split ($p < 0.001$). Prescriptions were 4 times more likely to be split if the prescribing physician's last statin prescription was split ($p < 0.001$). Likelihood of splitting was also significantly associated with the type of statin and the number of weeks-supply of drug dispensed.

The estimated cost savings from splitting statins in 2006 was \$2.35 million Canadian dollars (Table 4), or \$18 per statin patient. The potential avoided cost from splitting 20% of eligible statin prescriptions was \$10.5 million dollars, and the potential savings from splitting all eligible prescriptions was \$51.4 million dollars.

DISCUSSION

Our study showed clearly that patient, physician, and public drug coverage level characteristics were associated with splitting statins. An increasing trend in splitting over the study period coincided with market penetration of more expensive statins (atorvastatin and rosuvastatin), and increases in public drug plan cost-sharing levels that occurred in 2002 and 2003. Those policies are described in detail elsewhere (^{18,19}).

The relationship between patient age and splitting was not monotonic. For decades, public drug coverage in BC has been more generous for patients over 65 than for patients under 65. A correlation between better public coverage and older age most certainly accounted for some of the lower relative likelihood of splitting observed in older patients. Other factors such as frailty, cognitive impairment and concurrent use of other medications, which could make splitting inappropriate and which are more common in older patients, could also have contributed to the lower relative likelihood of splitting.

The observation that higher income patients were less likely to split than lower income ones was expected since lower income people have a greater need to save money. Females were more likely to split than males, and a test of interaction between female sex and income status showed that the combined effect was greater than the independent

effects, suggesting that at a given level of income females were more sensitive to the cost than males. This observation is similar to another study in BC on switching drugs as a consequence of reference pricing⁽²⁰⁾.

There were three results in our analysis that suggested physicians played a strong role in splitting decisions. The first was that most split prescriptions were prescribed by a small fraction of statin prescribers. The second was that the likelihood of a patient splitting was 4-fold greater if their physician's last statin patient also split. The third was that specialists were less likely to split than general practitioners (GP), perhaps because they would know less of their patients' ability to pay for drugs. The observation that most physicians do not split statins but that splitting is an acceptable and frequent practice for some physicians suggests that educational initiatives could increase the practice.

The generalizability of our results to other jurisdictions is unknown. The matter is complicated by the fact that drug insurance and drug prices vary substantially around the world. Our analysis also lacked information on private insurance coverage, which likely led to an underestimation of the effect of public drug coverage on splitting. Patients with private coverage and no public coverage would have less

of an incentive to split than patients with no coverage. In spite of these limitations, the direction of our effect estimates for insurance coverage should still translate to patients in other jurisdictions who are subject to flat (or substantially flat) prices for statins, and who pay a percentage of their prescription costs out-of-pocket.

For drug insurance plans that include a patient cost-sharing component, savings from tablet splitting can benefit both patients and the plan, and plans could influence splitting by using financial incentives. Some plans have recognized this and have adopted voluntary splitting programs. In the Veterans Affairs (VA) health care system in Palo Alto, California, for example, statin drug costs were lowered by 39%, including the cost of tablet splitters, among patients who volunteered for a splitting program (Error: Reference source not found). The savings were considerably large even though the VA purchased its drugs below wholesale prices. In that program, pharmacists were not compensated for any additional time they spent splitting tablets and educating patients, but additional pharmacist costs would easily have been covered by a fraction of the drug cost savings. In British Columbia, \$145.3 million dollars was spent on statins in 2006, \$123.8 million of which was for prescriptions that could have been split by patients who were not taking the largest strength and who were not on social income assistance or in a nursing home.

Pharmacists claimed \$12.2 million in dispensing fees for those prescriptions. Dispensing fees could have been doubled for every prescription that was split at a cost of less than one fifth of the savings in ingredient costs. Realistically, most patients could have split their own statins anyway. Other costs related to splitting, such as tablet splitters and ingredient waste, could also be expected to be small compared to the savings in drug costs.

Although most statins are not scored, evidence on splitting statins indicates that it is a simple and safe procedure for most patients. Some patients may not be good candidates because of frailty, cognitive impairment, or potential for incorrect dosing related to concurrent use of numerous drugs. Our analysis demonstrates that splitting has become more popular, and that potential savings are enormous. We believe that more physicians, pharmacists and patients should be made aware of this simple cost saving measure. Drug plans seeking ways to increase value for dollar should be exploring programs designed to markedly increase tablet splitting.

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Legend for Figures:

Figure 1: Trends in percent of statin prescriptions that were split in British Columbia

