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Increased health costs from mandated Therapeutic Substitution of proton pump inhibitors in British Columbia

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SUMMARY

Background
In 2003, British Columbia's PharmaCare programme implemented a drug reimbursement policy called Therapeutic Substitution, which required patients with acid-related diseases, primarily gastro-oesophageal reflux disease (GERD), to make a medically unnecessary switch from their prescribed proton pump inhibitor (PPI) to the cheapest available brand name PPI (Pariet, rabeprazole sodium), comprising a different (nongeneric) chemical.

Aim
To evaluate the independent effects of PPI Therapeutic Substitution on individual healthcare utilization among those complying with the policy.

Methods
We used the BC Ministry of Health Services' individual-level linked data, allowing isolation of healthcare utilization for the entire population of PPI consumers from 2002 to 2005.

Results
After controlling for individual case variation in age, gender and a proxy for pre-existing health status, regression analysis revealed statistically significant greater overall use of PPIs, physician services and hospital services independently associated with patients who complied with Therapeutic Substitution. Over the 3-year period 2003–2005, this represented net healthcare expenditures totalling approximately C$43.51 million (C$9.11 million in total PPI drug expenditures, C$24.65 million for physician services and C$9.75 million for hospital services).

Conclusion
Medically unnecessary drug switching caused by compliance with Therapeutic Substitution policy appears to be independently associated with higher overall healthcare utilization.

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INTRODUCTION

This study hypothesizes that if a patient, whose condition is stabilized on a prescribed medication regime, is forced to switch to a different medication, for no reason other than that their drug plan mandates the switch, then more frequent physician visits, diagnostic testing, hospital services and drug costs could result that, in aggregate, could increase overall healthcare costs.

Our supposition arose after the implementation of Therapeutic Substitution, a policy requiring British Columbians who were consuming proton pump inhibitor (PPI) medication to switch to the cheapest brand name PPI medication or risk loss of insurance coverage of the PPI under the provincial drug plan. During 2003–2004, many of these individuals contacted the Canadian Society of Intestinal Research, a registered charity with a patient-focused disease interest, complaining of destabilization of their acid-related diseases, primarily gastro-oesophageal reflux disease (GERD). Some reported a return of symptoms, such as severe heartburn and some reported side effects including diarrhoea, vomiting, nausea, chest pain, fatigue and, less commonly, vomiting blood. A number of these complaints required increased access to health care, leading us to suspect a change in health-related expenditures because of this policy.

The government of British Columbia (BC) administers separate public programmes providing insurance coverage for medical services (e.g. hospital and physician) and prescription drugs. All legal BC residents are eligible for publicly funded coverage of all hospital and physician services deemed to be medically necessary under the provincial medical insurance plan, with modest premiums and no co-payments or deductibles at point of service. In contrast, under the provincial prescription drug insurance programme, known since 2003 as Fair PharmaCare, coverage is also universal, but is subject to various deductibles on the basis of age and income. PharmaCare also uses a restricted formulary, stipulating which drugs are eligible for coverage.

Some history of the coverage of medications for acid-related diseases is relevant to this study. In 1995, BC PharmaCare implemented a Reference Drug Program (RDP) for first-line prescribing of several different therapeutic drug classes. The histamine-2 receptor antagonist (H_2RA) class, prescribed for acid-related disorders such as GERD, is subject to RDP. For H_2RAs, PharmaCare subsidizes the full cost of the least expensive drug (cimetidine) known as the ''reference'' drug. However, those consumers who fill prescriptions for drugs priced greater than the reference drug (i.e. ranitidine, nizatidine and famotidine) must pay the difference out-of-pocket. Under the Special Authority Program, PharmaCare allows physicians to apply on behalf of their patients, for full coverage of nonreference drugs, if the patients meet precise criteria.

Prior to July 2003, to qualify for a newer, more effective class of acid suppression, the PPI, a patient must have first failed to respond on cimetidine and then fail on another, nonreference H_2RA. At this point, a physician could have applied for Special Authority to prescribe any one of the existing brand name PPIs, which were, in order of their arrival on the Canadian market, Losec (omeprazole) (AstraZeneca, Canada Inc., Mississanga, Canada), Pantoloc (pantoprazole sodium) (Nycomed Canada Inc., Oakville, Canada), Prevacid (lansoprazole) (Takeda Pharmaceuticals America Inc., Lake Forest IL, USA), Nexium (esomeprazole magnesium) (AstraZeneca, Canada Inc., Mississanga, Canada) and Pariet (rabeprazole sodium) (Janssen-Ortho Inc., Toronto, Canada). There were no generic PPI drugs in the Canadian market at this time.

In a media release on 1 May 2003, the government of BC announced that it is 'providing a new PharmaCare coverage arrangement for patients with gastric ulcers and acid reflux disease that will ensure continued access to high-quality medication while protecting $42 million in PharmaCare resources over 3 years. The new arrangement, which takes effect July 15, affects the use of proton pump inhibitors'.[1]

This new arrangement, known as Therapeutic Substitution, varies significantly from the RDP. RDP allows a reimbursement level up to a specific cost level, equal to the cheapest medication in a class, whereas Therapeutic Substitution requires patients to switch their medication to the cheapest in the class to be eligible for coverage. Under Therapeutic Substitution, PharmaCare routinely only covers one medication in the PPI class. It is not possible for a consumer to pay for the difference between the designated substitute PPI and the one prescribed by their physician. If the consumer does not take the substituted PPI, then they have to pay out-of-pocket for the entire cost of the PPI prescribed by their physician. It is also important to note that this policy was the first of its

kind in Canada and PPIs were the only class involved.

Effective 15 July 2003, BC PharmaCare designated Pariet as the only PPI eligible for first-line public coverage. The result of Therapeutic Substitution policy was that all new patients requiring PPI treatment, after first failing on an H_2RA, had to accept Pariet or they would have to pay for the entire cost of the PPI drug out-of-pocket. It also meant that all persons who were stable on any of the other four PPI medications obtained previously under the Special Authority Program had to switch to Pariet or they would have to pay for the entire cost of the PPI drug out-of-pocket. A provision does exist for physicians to apply for Special Authority to have the cost of one of the other brand name PPIs covered, but only if the patient meets strict criteria, including treatment failure after an 8-week trial of Pariet (and a failure on H_2RA drugs before this).

The PharmaCare administrators did not conduct or reference any clinical trial that might have determined whether such mass switching could have produced negative effects for the patient population nor whether the various medications in this class would work the same way in each patient. BC PharmaCare deemed five bio-chemically dissimilar brand name products to be therapeutically equivalent and interchangeable. This policy is different from generic substitution, which is a common drug reimbursement policy mandating that consumers accept the cheaper, bio-chemically equivalent, generic version of a previously patented, brand name prescribed drug.

One additional factor is that also in 2003, the BC government introduced income-based deductibles for all drugs reimbursed under PharmaCare (Fair PharmaCare). However, under the Therapeutic Substitution policy, if the consumer remains on the nonsubstituted PPI and does not obtain Special Authority (i.e. permission from PharmaCare), then in addition to paying for the drug out-of-pocket, this private expenditure does not count towards the Fair PharmaCare plan deductible. Therefore, the Therapeutic Substitution policy financially penalizes the patient twice if they do not select the substitute PPI.

By providing PharmaCare coverage for only one brand name medication and not allowing consumers to pay the difference, as is the case under RDP, PharmaCare effectively generated mass switching of patients who were stabilized on one PPI to the substitute PPI.

MATERIALS AND METHODS

Data

We used data from BC's Linked Health Databases, including BC PharmaNet, obtained from the province's Ministry of Health Services under a request by Dr James Gray and the Canadian Society of Intestinal Research (CSIR). The databases were comprised of individual-level patient records for the entire population of the province in three separate databases: hospitals (Hospital Separations[2]), physicians' services (Medical Services Plan[3]) and prescription drugs (PharmaNet[4]). The hospital and physicians' databases reflect patient utilization that is almost entirely publicly funded. The PharmaNet database includes all prescription drug sales in the province, whether publicly or privately paid. Patient records can be linked across these databases because each patient is assigned an anonymous, unique numerical identifier that is the same for each database.

The Canadian Society of Intestinal Research's specific request included all patients who had filled a prescription for an H_2RA or PPI in each year. The PharmaNet data therefore only included fields showing prescriptions filled for H_2RAs or PPIs. It did not include prescriptions filled for other medications. This means that the data supplied by the Ministry of Health for this study contained individual level data on the utilization of hospitals, physician services and H_2RA and PPI prescriptions for all patients who filled a prescription for either an H_2RA or PPI during the years studied.

Method

The Ministry of Health Services creates a new record each time a patient is admitted to a hospital, receives a physician service or fills a prescription. This produces multiple records within the same year for those patients who make multiple uses of hospitals, physician services and/or prescription drugs. Our first step was to aggregate these multiple records into a single record for each patient within each year file. Then the aggregated single patient records within each year were merged across the three datasets to produce a single record for each patient within each year, containing any recorded use of hospitals, physician services and PPI drugs. We further narrowed the dataset by selecting only cases where patients filled a

Table 1. PPI patient population, by cohort, 2002–2005, British Columbia

Cohort	2002	2003	2004	2005
Therapeutic Substitution population (mixed prescriptions for Pariet and any other PPI)	1283	45 374	24 676	17 412
Pariet-only population	2155	29 622	84 088	103 174
Other PPI-only population	174 229	143 042	131 032	132 863
Total PPI (any brand) population	177 667	218 038	239 796	253 449

prescription within the year for any brand of PPI (cohort populations shown in Table 1).

Separate binary-coded variables were created to identify three groups (populations shown in Table 1) of patients taking PPIs:

(i) patients who only used Pariet and no other PPI (=1; all others = 0);

(ii) patients who used any other PPI except Pariet (=1; all others = 0); and

(iii) patients who had a mix of PPI prescriptions (Pariet plus any other PPI brand) within the year (=1; all others = 0). This latter group of patients with mixed drug regimens was assumed to have complied with Therapeutic Substitution by proxy.

Individual utilization of PPI drugs was defined by the total annual number of prescriptions (Rx) filled per patient. PPI utilization was observed separately for Pariet, as well as for other PPI brands, and a total for all PPI brands together was computed. Utilization of physician services was defined by the total annual number of fee-based medical services recorded per patient and the total annual cost of physician services per patient, based on the amounts recorded in the Medical Services Plan database. Individual hospital utilization was defined by the total annual number of hospital visits of any type per patient and the mean of the resource intensity weights (RIWs) assigned to each hospital visit (sum of recorded RIW values divided by the number of visits) per patient.

To estimate individual expenditures on PPI drugs (all brands) in each year, we created an expenditure variable using price and volume data sourced from IMS Health Canada Inc.[5] that was available from a previous study.[6] The data allowed us to calculate an average price (C$2003) per prescription for Pariet and also a volume-weighted average price per prescription across all other PPI brands. We then computed a variable for each patient's total annual PPI expenditures (TOTPPICOST) across all PPI brands by multiplying the number of prescriptions dispensed for Pariet and all other PPI brands per individual patient case by the relevant average price for each drug type. To estimate individual hospital expenditures (HOSPCOST), we first calculated the provincial average cost of a hospital visit using data published by the Canadian Institute for Health Information (CIHI)[7, 8] on total annual hospital expenditures and total annual hospital admissions of all types in the province of BC for 2003. This cost was assumed to be theoretically equal to a RIW of one (1). An expenditure variable was computed by multiplying the average 2003 province-wide cost per hospital visit by the mean RIW observed for each individual patient, producing a resource intensity-weighted estimate of the average cost of a hospital visit for each patient in each year. This result was then multiplied by the number of hospital visits recorded for each patient in each year. Annual individual expenditure on physician services was recorded in the database and did not require additional computations to produce a monetized total for each patient in each year.

We used SPSS software's (SPSS Inc., Chicago, IL, USA) OLS linear regression analysis to test for statistically significant relationships between the patient group identifier variable and individual case variation in any of our utilization and cost indicators within each year of study. We were specifically concerned with the relationship between the Therapeutic Substitution indicator (independent variable) and each utilization/cost indicator (dependent variable). Each regression test included additional independent variables for: year of birth (YOB) to control for the effect of age on individual utilization; for gender (SEX) to control for the effect of gender differences on individual utilization (binary variable 1 = male; 0 = female); and the same utilization variable in the previous year to control for independent effects of pre-existing health status by proxy.

Each cost variable was designated as the dependent variable in separate regression analyses producing an unstandardized beta-coefficient measured in currency units indicating the difference in annual expenditure on PPI drugs, physicians and hospitals in each year

statistically associated with each patient group identifier variable, after controlling for age, gender and our proxy for pre-existing health status. To estimate the total net costs independently associated with the mass switching generated by Therapeutic Substitution in particular, the beta-coefficients were multiplied against the number of Therapeutic Substitution patients in each year.

RESULTS

Cohort populations 2002–2005

Table 1 displays the annual population counts within each defined patient cohort from 2002 to 2005. The total number includes all patients filling one or more prescriptions within the year for any brand of PPI drug. The data show that the total PPI patient population was 177 667 in 2002 and rose steadily every year thereafter until reaching 253 449 by the end of 2005. The data show that a small number of patients had access to Pariet as early as 2002. The number of patients using Pariet exclusively (n = 2155) increased significantly following the full push of the drug to the market in 2003, rising ultimately to 103 174 patients by the end of 2005. Also, a number of patients (n = 1283) had switched between Pariet and other PPI brands in 2002 prior to the implementation of Therapeutic Substitution policy. The number of persons switching between Pariet and other PPI brands spiked at 45 374 in 2003, declining to 24 676 in 2004 and to 17 412 by the end of 2005.

Table 2. Regression results: therapeutic substitution cohort

	Unstandardized coefficients		Standardized coefficients		
Dependent variable	*B*	S.E.	Beta	*t*	Sig.
Total expenditure on PPI drugs (any brand) 2003	65.964	2.073	0.050	31.819	0.000
Total expenditure on PPI drugs (any brand) 2004	134.516	2.451	0.081	54.886	0.000
Total expenditure on PPI drugs (any brand) 2005	160.880	3.121	0.069	51.540	0.000
Total expenditure on physician services 2003	173.928	7.710	0.043	22.559	0.000
Total expenditure on physician services 2004	361.028	9.689	0.065	37.262	0.000
Total expenditure on physician services 2005	450.701	11.501	0.067	39.188	0.000
Total expenditure on hospital services 2003	24.387	6.309	0.008	3.866	0.000
Total expenditure on hospital services 2004	177.650	7.843	0.045	22.652	0.000
Total expenditure on hospital services 2005	244.485	9.333	0.051	26.196	0.000

Table 3. Regression results: Pariet-only cohort

	Unstandardized coefficients		Standardized coefficients		
Dependent variable	*B*	S.E.	Beta	*t*	Sig.
Total expenditure on PPI drugs (any brand) 2003	−75.691	2.381	−0.049	−31.785	0.000
Total expenditure on PPI drugs (any brand) 2004	−92.041	1.567	−0.087	−58.755	0.000
Total expenditure on PPI drugs (any brand) 2005	−48.405	1.641	−0.040	−29.505	0.000
Total Expenditure on Physician Services 2003	135.521	8.860	0.028	15.295	0.000
Total expenditure on physician services 2004	69.179	6.231	0.020	11.103	0.000
Total expenditure on physician services 2005	117.119	6.012	0.034	19.479	0.000
Total expenditure on hospital services 2003	22.944	7.308	0.007	3.139	0.002
Total expenditure on hospital services 2004	43.814	5.037	0.018	8.699	0.000
Total expenditure on hospital services 2005	104.196	4.871	0.042	21.393	0.000

Table 4. Regression results: other PPI-only cohort

	Unstandardized coefficients		Standardized coefficients		
Dependent variable	*B*	S.E.	Beta	*t*	Sig.
Total expenditure on PPI drugs (any brand) 2003	−5.918	1.724	−0.005	−3.433	0.001
Total expenditure on PPI drugs (any brand) 2004	34.301	1.518	0.034	22.599	0.000
Total expenditure on PPI drugs (any brand) 2005	4.141	1.618	0.004	2.560	0.010
Total expenditure on physician services 2003	−196.700	6.495	−0.056	−30.285	0.000
Total expenditure on physician services 2004	−203.918	6.017	−0.061	−33.888	0.000
Total expenditure on physician services 2005	−232.857	5.912	−0.068	−39.387	0.000
Total expenditure on hospital services 2003	−29.717	5.339	−0.012	−5.566	0.000
Total expenditure on hospital services 2004	−108.791	4.853	−0.045	−22.415	0.000
Total expenditure on hospital services 2005	−165.510	4.789	−0.068	−34.563	0.000

Tests of statistical significance

Regression output tables are available online (Appendices S1, S2 and S3). Tables 2–4 summarize the key regression results for cost-associated independent variables. Our analysis found a statistically significant and positive correlation between greater overall use of PPI prescriptions, physician services and hospital visits, creating independently associated costs for patients who complied with the switching requirement of Therapeutic Substitution policy (Sig. = 0.000; i.e. >99% confidence level) after controlling for variation in the YOB, gender (SEX) and pre-existing health status in each model. All results are consistent across all years. Unstandardized beta-coefficients are stated in dollar variations independently associated with the Therapeutic Substitution indicator, after controlling for the effect of age, gender and pre-existing health status. The regression results provide the basis for a reasonable upper-limit estimate of any net costs shown to have been independently associated with the implementation of Therapeutic Substitution policy in BC.

PPI expenditures

Net PPI expenditures were estimated by applying the unstandardized beta-coefficient (*B*) results of our regression analysis. The unstandardized beta-coefficient produced for 2003 is proportionally much smaller than in 2004 and 2005, probably because it represents only the half-year impact of Therapeutic Substitution, which was implemented in July 2003 (this observation applies to other cost estimates as well). Stated in C$2003, the data show (Table 5) that the greater use of PPI drugs statistically associated with the impact of Therapeutic Substitution policy, would have produced a net annual expenditure

Table 5. Health costs independently associated with patients who complied with Therapeutic Substitution (TS): controlling for age, gender and utilization in previous year, 2003–2005

	2003	2004	2005	Row totals
TS POP	45 374	24 676	17 412	–
TS-associated variance TOTPPICOST	$65.96	$134.52	$160.88	–
Subtotal	$2 992 869	$3 319 416	$2 801 243	$9 113 527
TS-associated variance PHYSCOST	$173.93	$361.03	$450.70	–
Subtotal	$7 891 900	$8 908 776	$7 847 588	$24 648 265
TS-associated variance HOSPCOST	$24.39	$177.65	$244.49	–
Subtotal	$1 106 672	$4 383 691	$4 257 060	$9 747 423
Total cost	$11 991 441	$16 611 883	$14 905 891	$43 509 215

increase of $2.99 million in total for 2003 when extrapolated across the identified population of Therapeutic Substitution patients in that year. The corresponding difference in net PPI expenditures across the population of Therapeutic Substitution patients was $3.32 million in 2004 and $2.80 million in 2005. Total net PPI expenditures associated with patients affected by Therapeutic Substitution policy across all 3 years was approximately $9.11 million.

Physician expenditures

Net physician costs (Table 5) were estimated by again applying the unstandardized beta-coefficient (*B*) results of our regression analysis. The unstandardized beta-coefficient scores from the regression analysis suggest that there were greater average expenditures on physician services statistically associated with Therapeutic Substitution patients. When extrapolated across the identified Therapeutic Substitution patient population in each year, our results suggest the introduction of Therapeutic Substitution policy produced a net cost of $7.89 million in 2003, $8.91 million in 2004 and $7.85 million in 2005, for a total of $24.65 million over all 3 years (C$2003).

Hospital expenditures

Net hospital costs (Table 5) were also estimated by applying the unstandardized beta-coefficient (*B*) results of our regression analysis to the size of the PPI population affected by Therapeutic Substitution in each year. When extrapolated across the identified Therapeutic Substitution patient population in each year, our results suggest the introduction of Therapeutic Substitution policy produced net hospital costs of $1.11 million in 2003, $4.38 million in 2004 and $4.26 million in 2005, for a total of $9.75 million over all 3 years (C$2003).

Other findings

Although we did not do a PPI-to-PPI randomized clinical trial, our results show (Tables 2–4) some utilization differences between groups of PPI consumers. The highest utilization of physician and hospital services was associated with the population identified as the Therapeutic Substitution cohort, followed by persons consuming Pariet exclusively, and, finally, those persons who were taking any PPI other than Pariet had the lowest utilization of physician and hospital services.

DISCUSSION

Conclusions

Our study finds that the 2003 implementation of Therapeutic Substitution policy for PPIs in BC probably generated significant direct, avoidable, net healthcare costs over the period 2003–2005, potentially totalling up to $43.51 million. Our findings of higher utilization are generally consistent with other recent research suggesting that there were significant adverse health reactions correlated with the implementation of Therapeutic Substitution policy in October 2005 by the Canadian federal government for drug programmes under its First Nations and Inuit Health Branch.[9]

In contrast, in earlier research, Schneeweiss *et al.*[10] estimated net savings specifically to the BC PharmaCare programme of approximately $2.9 million (C$2003) resulting from PPI Therapeutic Substitution policy in the first 6 months following its July 2003 introduction. In accounting for the differences between our estimate and the estimate provided by Schneeweiss *et al.*, it is important to note the following:

(i) The Schneeweiss *et al.* study was restricted to patients over the age of 65 years, whereas our study included the entire population of patients who filled a prescription for a PPI in each year across all ages.

(ii) Schneeweiss *et al.* studied monthly variation in individual utilization in 2003. In contrast, we studied annual variation in individual utilization in 2003, 2004 and 2005.

(iii) Schneeweiss *et al.* reported that they did not observe any monthly utilization changes associated with hospital services specifically related only to gastrointestinal haemorrhage during the period, but they did observe temporary increases in the monthly utilization of physician services, though they did not report the associated costs because they deemed these to be statistically insignificant. In contrast, we observed statistically significant differences in the overall annual individual utilization of PPI drugs (total), hospitals and physician services among patients affected by Therapeutic Substitution and calculated costs across this population.

Schneeweiss *et al.* estimated savings to the publicly funded PharmaCare plan only and therefore did not count any cost shifting from PharmaCare to individuals

or private supplementary insurers that occurred because of the interaction of coverage eligibility rules under Therapeutic Substitution policy and the implementation of deductible limits under PharmaCare. Due to the coincidental introduction of income-based deductibles under Fair PharmaCare in 2003, a large part of the gross savings to the provincial public payer assumed by BC policy makers, would have resulted from shifting costs directly onto patients, and could not be attributed entirely to price savings from Therapeutic Substitution estimated by Schneeweiss *et al*. In addition, for patients who choose to remain on their prescribed PPI instead of switching to the provincially mandated Pariet, the entire cost of their prescriptions shifts to out-of-pocket expenditures with introduction of the deductible, because none of these out-of-pocket expenses would have counted towards the PharmaCare deductible. In contrast with Schneeweiss *et al.*, our study measured net changes in expenditures across the entire market including publicly and privately funded PPI prescriptions.

Any projected reductions in PharmaCare expenditures based on Schneeweiss *et al*. in 2003 would also have been overestimated because the savings they calculated were temporary. This is because the reduction in costs resulting from the substitution of Pariet at a lower price, could only last until the existing patents on the various other brand name PPIs expire. As generic copies of those drugs enter the market, they will automatically become substitutes for the applicable brand name product (same chemical structure) under existing PharmaCare policies. Our study did not investigate the date at which the patents expire on competing nonsubstituted PPI drugs. However, at least one generic PPI (Apo-omeprazole) had captured a significant and growing share of the national market by the end of 2004. Available data indicate that the average prescription price for this generic in 2003 ($61.97) was roughly the same as for Pariet ($57.54) in the same year.

Any savings estimated from Schneeweiss *et al*. could not be wholly attributed to Therapeutic Substitution policy. There is no way to know how many patients would have voluntarily chosen to switch to, or start on Pariet in the absence of Therapeutic Substitution policy and so there is no way to estimate the savings that occurred exclusively as a direct result of the policy.

Our empirical findings appear to undermine one of the basic rationales for Therapeutic Substitution, which is cost savings. In order for Therapeutic Substitution to be justified, any public savings from the policy must significantly outweigh the public and private additional costs of increased use of medical goods and services that could arise when physicians' prescribing advice is ignored and patients' choice is diminished. It is not enough for the savings from substitution merely to offset increases in other healthcare costs. It is even worse if substitution policy results in additional net healthcare costs, as our study suggests actually occurred in BC among persons taking PPIs. The evidence presented in this study suggests (with cautions noted below) that Therapeutic Substitution policy for PPIs in BC was statistically associated with significantly greater individual use of health care by the patients affected by the policy, that the effect was probably independent of confounding variables and that the effect was large enough to create net costs at the aggregate level.

Limitations

This study's design does not permit direct comparisons of drug efficacy among potential therapeutic substitutes nor did it permit us to determine whether changes in utilization were related to efficacy differences between PPI brands.

By proxy, we assumed that patients with mixed PPI prescriptions (Pariet plus any other PPI brand) during the year had 'switched' PPI brands in compliance with Therapeutic Substitution. It is possible that some patients could have switched for reasons unrelated to the policy. We also could not determine the direction of the switching.

Our regression model controlled for healthcare utilization in the previous year as a proxy for independent effects of pre-existing health status on the observed utilization differences between cases. It was not possible to measure independent health status effects arising only within the current year because of co-linearity between available proxy variables for health status and actual health utilization variables in the same year. However, only those patients who were expecting in advance that their expenditures would exceed the deductible threshold would face stronger incentives to comply with Therapeutic Substitution than would other patients. We believe that it is unlikely that this incentive would have been sufficiently apparent to patients whose health status changed independently of Therapeutic Substitution within the year.

In addition, under the Special Authority provisions, patients with greater known health risks would have been able to avoid the requirement to switch medications, making these patients less likely to be included in our test population.

Our model did not include a variable that controlled for the socio economic status of patients because case-specific income data were unavailable. This could be important because while eligibility for benefits under BC's Fair PharmaCare programme is universal for legal residents of the province, coverage is still subject to income-dependent deductibles based on a sliding scale.[11] In practice, most people obtain private supplemental insurance coverage as an employer-provided benefit for any expenses that would occur below the Fair PharmaCare deductible threshold. These people would not necessarily have a financial incentive to comply with PharmaCare's Therapeutic Substitution policy unless their private plan had similar rules. Therefore, the unemployed and those employed but without supplemental drug insurance as a benefit of their employment would probably disproportionately represent those who complied with the switching requirement. However, some of the latter group would have been self-employed (e.g. professionals, small business owners) and would probably be disproportionately represented by relatively higher income earners. In addition, our results show that higher utilization of physician and hospital services was also independently associated with PPI patients who used Pariet exclusively, but the unstandardized beta-coefficient scores for this group were lower than the utilization associated with those who switched drug regimens. If lower socio economic status created greater incentives to comply with Therapeutic Substitution for patients, then these factors would have been present for both groups of Pariet users, as would any associated variation in health status linked to socioeconomic status. The difference between the unstandardized beta-coefficients for the two groups who used Pariet reinforces our finding that there was an independent effect from the switching caused by Therapeutic Substitution policy, which was not confounded by variation in socioeconomic status between cases. Knowing this and given that our datasets cover the entire population and our models included control variables for age, gender, and a proxy for pre-existing health status, we believe that the addition of a control variable for individual socioeconomic status would not probably affect the reliability of our results. However, we acknowledge the possibility as a caution when interpreting our results.

For patients who used Pariet exclusively, unstandardized beta-coefficients generally showed decreased PPI expenditures, but increased overall expenditures on physician and hospital services for this group of patients. However, it is unknown how many patients voluntarily selected Pariet and how many were required to do so as a result of Therapeutic Substitution policy and so it is impossible to isolate costs resulting from the policy itself for this cohort.

The available data did not permit an estimate of the impact of Therapeutic Substitution on overall prescription drug use or on personal spending for over-the-counter products or on any other private spending that might have occurred as a result of any unmeasured changes in health outcomes. In addition, while data were available, this study did not measure utilization changes in H_2RA drug use. CSIR's patient experience suggests that where utilization changes did occur, this would have resulted in uncounted additional costs, not savings.

This study also did not estimate broader socioeconomic costs such as productivity or efficiency losses or effects on other family members that could be associated with the additional healthcare utilization for our patient cohort. We did not examine distortions in the delivery of physician services, such as any potential extra staffing costs required to handle an increased number of Special Authority requests to BC PharmaCare or PharmaCare's extra costs in processing these requests. We also did not examine crowding-out effects on other patients from the increased utilization of healthcare resources among PPI switchers.

We assumed that physician fees for service did not change over this period and are therefore stated in dollar values that are comparable to the constant C$2003 currency figures used for PPI and hospital cost estimates. This would not have affected the validity of our results regarding individual differences in expenditure on physician services occurring within the same year.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Volume-weighted average prescription prices, by PPI brand, Canada, 2003.

Appendix S2. Estimated number of hospital visits in British Columbia, 2002–2003 and 2003–2004.

Appendix S3. Estimated average cost per hospital visit, British Columbia, 2003.

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