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**The Impact of Reference Pricing of Cardiovascular Drugs
on Health Care Costs and Health Outcomes: Evidence
from British Columbia – Volume I: Summary**

**Paul V. Grootendorst, Lisa R. Dolovich,
Anne M. Holbrook, Adrian R. Levy,
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SEDAP Research Paper No. 70

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**THE IMPACT OF REFERENCE PRICING OF CARDIOVASCULAR
DRUGS ON HEALTH CARE COSTS AND HEALTH OUTCOMES:
EVIDENCE FROM BRITISH COLUMBIA – VOLUME I: SUMMARY**

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Abstract

The Impact of Reference Pricing of Cardiovascular Drugs on Health Care Costs and Health Outcomes: Evidence from British Columbia – Volume I: Summary

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Objective: We estimate the effects of Reference Pricing, a drug cost control policy introduced by the BC Ministry of Health Pharmacare program in 1995, on its program expenditures for seniors, out of pocket costs paid by its senior beneficiaries, indicators of beneficiary health status and attendant Ministry of Health expenditures on physicians and hospitals services. **Rationale:** Reference pricing (RP) limits the reimbursement of a group of drugs with similar therapeutic effect but different active ingredients to a fixed "reference price". The setting of the reference price varies by jurisdiction but typically is based on an average of the lowest cost "reference standard" drugs within the group. Critics of RP contend that the partially subsidized and fully subsidized (reference standard) drugs are not therapeutically interchangeable, and therefore patient health will be compromised and use of other non-pharmacologic health services may increase as a result, thus partially or wholly offsetting any potential cost savings from the policy.

Findings: The application of RP to 3 groups of cardiac drugs produced annualized savings to Pharmacare of about \$7.7 million, or 3.6% of the \$213.7 million that Pharmacare spent on drugs for seniors (not including dispensing fees) in 1997. The additional costs for physician consultations were modest, around \$500,000 in the subsample of seniors we studied, from the introduction of the RP plans to March 1998, although the costs could be greater, perhaps up to twice this amount, if we accounted for all seniors exposed to the RP over the same period. We found no effects of RP on mortality, or premature admission to a longterm care facility.

Seniors using the nitrate drugs for angina that were no longer fully subsidized when RP was introduced faced a higher probability in the short run of using medicines to deal with acute exacerbations of angina and in the longer run having bypass surgery or other revascularization procedures. No long run effects of morbidity were observed for the application of RP to two different types of anti-hypertensive medications, although there was a short run increase in the rate of revascularizations among those taking 1 type of anti-hypertensive: the ACE inhibitors. The results of these morbidity models should be seen as tentative, until these results can be replicated using alternative estimation strategies.

Conclusions: The introduction of RP can indeed reduce Ministry of Health drug expenditures. The effects of RP on patient morbidity remain to be fully investigated before definitive policy recommendations can be offered.

Health Transitions Fund Project NA222:

The impact of reference pricing of cardiovascular drugs on health care costs and health outcomes: evidence from British Columbia

Volume I: Final Report to HTF

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Key words: reference pricing, reference based pricing, prescription drugs, utilization, ACE inhibitors, calcium channel blockers, nitrates, pharmaceutical cost control, seniors, copayments, charges, user fees, costs

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1 EXECUTIVE SUMMARY

1.1 Purpose of the project

Reference pricing (RP) has been adopted both domestically and internationally as a means of limiting expenditures on drug subsidy and insurance programs. RP limits the reimbursement of a group of drugs with similar therapeutic effect but different active ingredients to a fixed ‘reference price’. The setting of the reference price varies by jurisdiction but typically is based on an average of the lowest cost ‘reference standard’ drugs within the group. Drug program beneficiaries have the option of paying the difference between the retail price and the reference price for partially subsidized drugs.

The introduction of RP by the British Columbia Ministry of Health Pharmacare program, the provincial government drug subsidy program for seniors and others, has generated considerable controversy. Critics of RP contend that the partially subsidized and fully subsidized (reference standard) drugs are not therapeutically interchangeable, and therefore patient health will be compromised and use of physicians’ and hospital-based health services may increase as a result, thus partially or wholly offsetting any potential cost savings from the policy. The RP policy, however, has provisions that allow selected patients to be exempted from the policy.

There is only limited evidence regarding the effects of RP policies introduced internationally. Moreover, the existing evidence may not necessarily be generalizable, owing to differences in the design of the RP policies. We therefore conducted an evaluation of the RP policy as implemented by BC Pharmacare to the nitrates, angiotensin-converting-enzyme (ACE) inhibitors and dihydropyridine calcium channel blockers (CCBs). We investigated whether RP has reduced Pharmacare drug expenditures without adversely affecting patient health status (either mortality or morbidity) or increasing expenditures on physicians’ and hospital-based services. We also investigated the following distributive effects of the policy: How much did patients collectively pay for the partially subsidized “Restricted” drugs? Did patients’ access to the Restricted drugs depend on their ability to pay?

1.2 Target Audience

Drug plan managers, both public and private, health policy makers, consumers, pharmaceutical manufacturers, clinicians and scientists should find this report useful.

1.3 Methodology

Using quasi-experimental methods, we focused on the effects of RP on senior (65+ years) beneficiaries of the BC Pharmacare program. To investigate the effects of RP on drug costs, we assembled monthly claims data, aggregated across all senior beneficiaries, on the drug groups targeted by RP, and examined the pre-post RP changes in prescribing volumes, Pharmacare reimbursement and patient expenditures for these drugs.

We used longitudinal patient-level data to estimate the effects of RP on morbidity and non-drug health care expenditures. First, we defined two groups of Pharmacare senior beneficiaries who

were and were not exposed to the RP policy. The former group includes those who, prior to the introduction of RP, were continuous users of drugs that were only partially reimbursed under RP, and the latter consist of those who, again prior to the introduction of RP, were continuous users of drugs that remained fully reimbursed under RP. We then estimated the pre-post RP changes in indicators of morbidity (hospital admissions for cardiovascular disease, and associated length of stay, revascularization, prescriptions of sublingual nitroglycerin, physician hospital and emergency room consults, physician ambulatory consults, surgical and diagnostic physician services related to cardiovascular disease) and health care costs (physician and hospital-specific) of those beneficiaries exposed to RP. The corresponding changes for beneficiaries not exposed to RP were used to control for secular trends. These models estimate the average health effect among a variety of subjects who might differ in the way their health changed after the policy. We distinguished between the short run vs long run effects of the RP policy. Shortrun effects occurred within the first 4 months of the implementation of the policy; long run effects occurred from the introduction of the policy to the end of the sample period, March 1998.

We also used patient-level data to estimate the effects of RP on death due to cardiovascular disease and time to admission to a longterm care facility. These were estimated using survival models in which we compared time-to-event for those exposed and not exposed to RP, while directly controlling for confounding variables, i.e., variables that are associated with both survival and RP exposure status. To ensure results were robust, we compared the survival differences between those exposed and not exposed to RP during the year *prior* to the introduction of RP. This quantity isolates the influence of confounding variables and was used to adjust the survival differences between those exposed and not exposed to RP during the year after the introduction of RP.

To obtain a Restricted drug after the introduction of RP, Pharmacare beneficiaries could either pay the additional charge or receive an exemption, in which case Pharmacare paid the additional charge. Using patient-level data, we modeled how senior's income status (an indicator of low income) affected both the probability of exemption from RP, and, in the subsample of seniors who were not exempted, both the probability of any payment and the amount paid for Restricted drugs. If RP adversely affected patient health status, then assessing the extent to which income improved access to Restricted drugs provides evidence about the equity of this policy.

1.4 Main findings

1.4.1 *Drug costs and use*

We estimate that RP of the nitrates, ACE inhibitors and CCBs drug classes reduced Pharmacare expenditures on its seniors drug plan by \$23.8 to \$24.8 million (depending on the estimation method used) between October 1995 to May 1999. This translates into annualized savings to Pharmacare of approximately \$7.7 million, or 3.6% of the \$213.7 million that Pharmacare spent on drugs for seniors (not including dispensing fees) in 1997. Approximately 24% of Pharmacare's savings represent additional costs to seniors who elected to pay for the higher cost drugs.

The estimate of the effect of the introduction of RP on savings on the CCB drugs includes the savings attributable to the concurrent introduction of the policy that limited reimbursement of the sustained release versions of verapamil and diltiazem to the equivalent dosage strengths of the regular release versions. Not included are the savings attributable to the application of RP to other drug groups or to other Pharmacare beneficiaries, including welfare recipients and those with large drug costs relative to income.

1.4.2 Mortality

Using conventional statistical methods, we found no evidence of an increase in rates of mortality associated with cardiovascular or renal disorders after RP was applied to the nitrates, ACE inhibitor and CCBs drug classes.

1.4.3 Morbidity and physician costs

Using conventional statistical methods, we found no evidence of an increase in the rates of longterm care admissions after RP was applied to the nitrates, ACE inhibitor and CCBs drug classes.

The use and expenditures on ambulatory physician consultations increased after the implementation of the policy, likely due to the fact that many seniors needed to consult with their physicians to discuss treatment options (e.g. switch to a fully subsidized drug, apply for an exemption), and to monitor the progress of those who switched drugs. The increased visits could have been due to changes in patient morbidity as well. Physician consultation rates for ACE inhibitor users increased 11% within 15 months after the introduction of RP; the corresponding figure for CCB users was 7%. Among nitrate users, additional visits were concentrated in the first 4 months of the policy; visits increased by 9%, but this was offset by a subsequent reduction in visits. We found that the additional costs for physician consultations to be modest, around \$500,000 in the subsample of seniors we studied, from the introduction of the RP plans to March 1998. Because we did not focus on all seniors potentially affected by RP, actual additional costs could be greater, perhaps up to twice this amount.

Sublingual nitroglycerin is used to control acute exacerbations of angina and was used as a marker for patient health status. Seniors using the nitrate drugs for angina that were no longer fully subsidized when RP was introduced faced a higher likelihood of using sublingual nitroglycerin in the first 4 months of RP. These subjects also had a higher likelihood of bypass surgery or other revascularization procedure in the longer run. No such effects of morbidity were observed for the application of RP to ACE inhibitors or CCBs, although there was an increase in the rate of revascularizations among those taking ACE inhibitors, in the first 4 months after the policy only. The results of these morbidity models should be seen as tentative, until these results can be replicated using alternative estimation strategies. For this reason the costs of the revascularization and related services were not estimated.

1.4.4 *Effect of income on access to the partially subsidized 'Restricted' drugs*

We found that among those using ACE inhibitors or CCBs, those with low income had the same probability of exemption as did those with high income. Among nitrates users, those with low income were at least 2% more likely to be exempted than those with high income. Among the subsample of those not exempted from RP, low income status had some effect on the probability and amount paid. Those with low income were between at least 4-5% less likely to pay more than \$1 for Restricted drugs over the year following the introduction of RP. Of those that did pay more than \$1, low income seniors paid between at least \$6.48 to \$10.88 less than did higher income seniors. These represent proportional reductions of between at least 6%-14%, depending on the drug class (12% for nitrates, 6% for ACE inhibitors, 14% for CCBs). The interpretation of these figures is that low income seniors who do not receive continuous exemptions from RP use slightly fewer Restricted drugs post policy and hence are more likely to switch to a fully subsidized drug, or reduce or discontinue drug use. Hence for those seniors who are not exempted from RP, there is some evidence of income-based impediments to access for the Restricted drugs, although the impediments do not appear to be particularly large.

1.5 Recommendations and policy implications

From the perspective of the BC Ministry of Health, a comprehensive assessment of the RP policy requires quantification of all of its costs and benefits. This study estimates the benefits but not all of the costs of the introduction of the RP policy to senior Pharmacare beneficiaries. On the benefits side, we estimate that the application of RP to the nitrates, ACE inhibitor and CCB drugs was associated with a reduction in expenditures on its seniors drug plan in the order of \$24 million as of May 1999. On the other side of the ledger are the additional expenditures on ambulatory physician consultations (likely under \$1 million), and the costs of the additional revascularization procedures, and the cost of the additional sublingual nitroglycerin dispensed to nitrates users. We have not yet estimated all of these costs because of uncertainty as to the validity of our models. A full assessment would also need to incorporate the costs of administration of the RP program (the additional staff required to handle exemption requests, for example).

2 OBJECTIVES AND RELEVANCE OF PROJECT

Reference pricing (RP) has been adopted both domestically (British Columbia and Nova Scotia) and internationally (USA, Australia, New Zealand, Germany, and elsewhere) as a means of limiting expenditures on drug subsidy and insurance programs. RP limits the reimbursement of a group of drugs with similar therapeutic effect but different active ingredients – each of the non steroidal anti-inflammatory drugs for example – to a fixed ‘reference price’. The setting of the reference price varies by jurisdiction [1;2] but typically is based on an average of the lowest cost ‘reference standard’ drugs within the group. Drug program beneficiaries have the option of paying the difference between the retail price and the reference price for partially subsidized drugs.

The introduction of RP by the British Columbia Ministry of Health Pharmacare program,¹ the provincial government drug subsidy program for seniors and others, has generated considerable controversy [3-7]. Moreover, the limited evidence regarding the effects of RP policies introduced internationally, coupled with the limited generalizability of these findings, has done little to settle the debate. This report investigates whether RP, as applied to the nitrates, angiotensin-converting-enzyme (ACE) inhibitors and dihydropyridine calcium channel blockers (CCBs), has reduced Pharmacare drug expenditures without adversely affecting patient health status (either mortality or morbidity) or increasing non-pharmaceutical health care expenditures. We also investigate the distributive effects of the policy: How much did Pharmacare beneficiaries pay for the partially subsidized “Restricted” drugs? And did beneficiaries’ access to drugs depend on their ability to pay? Finally, we present the findings of a literature review of the therapeutic equivalence of the ACE inhibitors and the CCBs.

Critics of RP contend that the partially subsidized (Restricted) and fully subsidized (reference standard) drugs are not therapeutically interchangeable, and therefore patient health will be compromised and use of other non-pharmacologic health services may increase as a result, thus partially or wholly offsetting any potential cost savings from the policy [7-11]. Pharmacare will, however, exempt patients who might not tolerate a switch in medicines. RP could also adversely affect health if switching between Restricted and reference standard drugs is harmful, or if those who do not switch instead pay out of pocket and, in an attempt to save money, unwittingly decrease the use of the Restricted drug below the point where it ceases to provide full therapeutic effect.

The RP policy could also increase health care costs for reasons unrelated to patient health. First, patients taking a drug that is no longer fully reimbursed might consult their physician about treatment options, thus increasing the number of physician visits, as would the monitoring of patients whose medication has been switched [8]. Second, physicians, pharmacists and patients incur the time and other costs in complying with the policy²; this is in addition to the direct costs of program administration [6;8;12].

¹ Information on Pharmacare’s programs can be found at:
<http://www.moh.hnet.bc.ca/pharme/outgoing/PcareTrends2000.pdf>

² Anecdotal reports suggest that the initial implementation of RP was met with much opposition among physicians and pharmacists alike. Apart from the time costs of explaining the policy to patients, and filling out exemption

The ability of RP to reduce Pharmacare program expenditures is also controversial. Given that drug prices within a group deemed therapeutically interchangeable can vary substantially, limiting reimbursement to the cost of the lowest priced drugs should reduce costs. But there may be offsetting factors. First, Pharmacare does not save money on beneficiaries who are exempted from the policy. Second, physicians might substitute relatively expensive drugs that are used for the same indication but not directly targeted by the RP policy [1;2;12;13]. For example, during the 3 month period following the RP of nitrates, the average cost to Pharmacare per daily dose of the lowest cost CCB, an alternative to nitrates for the management of angina, was greater than all but 1 of the nitrates. Third, economic theory suggests that setting reimbursement rates on the basis of the prices of a set of reference standard drugs might encourage the manufacturers of these drugs to raise prices, although this might be offset by reductions in the prices charged by manufacturers of partially subsidized drugs [14-17]. Fourth, patients whose angina was worsened by the nitrates RP policy might use more acute 'rescue' therapy, the first line of which is sublingual nitroglycerin, resulting in additional drug expenditures. Finally, to the extent that RP is effective in reducing insurers' expenditures, it might do so by shifting costs to beneficiaries who pay the difference between the retail price and the reference price [18].

Drug manufacturers have also criticized the RP policy on grounds that any reductions in their revenues, which are identically the cost savings to BC Pharmacare, will lessen the incentive to invest in research and development activities. From a financial point of view, it is unclear whether the decreased revenues in BC will affect the profitability of future research activities. Sales to the beneficiaries of the BC Pharmacare program, after all, constitute a small share of the national drug market and a miniscule share of the global market. On the other hand, if all jurisdictions impose RP, then the impact on revenues might be substantial. And the likelihood that other jurisdictions will impose RP depends, in part, on the success of the RP policy implemented in BC.

To date, the evaluations of the effects of RP policies introduced in jurisdictions outside BC have focused on the impact of RP on drug costs. Because the drug cost studies are typically descriptive in nature [17], and often do not control for confounding effects [19;20] the conclusions drawn from them are tentative. These studies generally conclude, however, that RP is largely ineffective in controlling drug costs [2;12;13;18;21-23]. There has been much less research into the effects of RP on patient health. Thomas, Mann and Williams [24], and Thomas and Mann [25] examined the clinical outcomes of 126 patients in New Zealand who switched from a partially subsidized to a fully subsidized medication for blood lipid control, (i.e., simvastatin to fluvastatin) after the public drug insurer introduced RP for these drugs in 1997. The overwhelming majority (94%) of switchers experienced an increase in blood lipid levels [24], relative to their pre-policy levels and there was a tripling (from 9 to 27) in the number of adverse thrombotic vascular events, such as unstable angina, strokes and myocardial infarction in the six month period after the introduction of RP compared to the previous 6 month period [25]. This research has been questioned, however, because of the possibility that factors other than RP were responsible for the apparent increase in vascular events after the introduction of the policy. These confounding factors include changes in clinical management of patients or changes in

forms, some health care providers viewed the imposition of RP as an affront on their clinical decision making autonomy.

patient compliance [26], and the effects of attrition bias [27]: The subjects sampled before the introduction of RP (i.e. when they were taking simvastatin) had to have been healthy enough to avoid death. A similar restriction was not in effect after subjects switched medications. Hence the increase in adverse event rates after the introduction of RP might have been overstated.

Irrespective of the quality of the evidence of the effects of RP policies introduced internationally, the evidence may not necessarily be generalizable to the RP policy implemented in BC. First, there are substantial differences in the design of RP policies, such as how low the reference price is set, the groups of drugs subject to the reimbursement restrictions, and the mechanisms by which patients can be exempted from them, if at all [1;17]. Second, even if the RP policy introduced in BC was identical to those introduced elsewhere, one might expect differences in the effects of the policies owing to differences in drug prices and the patterns of prescribing of drugs. For example, the potential savings from RP depends on the spread between the highest priced drug and the maximum reimbursement price set by the Ministry of Health in the drug categories targeted by the policy: The bigger the spread, the bigger are the potential savings. The spread in prices, in turn, depends on jurisdiction-specific factors such as the availability of generic drugs, direct price regulation and the length of patent protection afforded to patent-protected drugs. Potential savings from RP are also higher, the more frequently the higher priced drugs are prescribed. Prescribing patterns also are jurisdiction specific, as they depend on local regulations such as formulary restrictions, mandatory generic substitution, and the use of physician drug budgets, as well as factors such as the influence of physician opinion leaders.

This report investigates whether RP, as applied to the nitrates, angiotensin-converting-enzyme (ACE) inhibitors and dihydropyridine calcium channel blockers (CCBs), has reduced Pharmacare drug expenditures without adversely affecting patient health status (either mortality or morbidity) or increasing non-pharmaceutical health care expenditures. We also investigate the distributive effects of the policy: How much did Pharmacare beneficiaries pay for the partially subsidized “Restricted” drugs? And did beneficiary’s access to drugs depend on their ability to pay? Finally, we present the findings of a literature review of the therapeutic equivalence of the ACE inhibitors and the CCBs.

The plan of this report is as follows: in section 3, we describe the project activities, including our research design and methods. Section 4 summarizes the findings and presents some policy implications. The dissemination plan for this work is outlined in Section 5. The 2 volumes accompanying this volume contain a comprehensive description of the RP policy, our methods and results (volume II), and a review of the clinical evidence regarding the therapeutic equivalence of the different ACE inhibitors and CCBs (volume III).

3 PROJECT ACTIVITIES

Using quasi-experimental methods, we estimated the effects of RP on senior (65+ years) beneficiaries of the BC Pharmacare program. To investigate the effects of RP on drug costs, we assembled monthly claims data, aggregated across all senior beneficiaries, for the drug groups targeted by RP, and examined the pre-post RP changes in prescribing volumes, Pharmacare reimbursement and patient charges for these drugs. In this exercise, we did not have access to a comparator group that remained unaffected by RP, which would have allowed us to control for time-varying confounders. We instead examined the sensitivity of our estimates to assumptions regarding secular changes in prescribing pre-post RP.

We used longitudinal patient-level data and the ‘difference in differences’ design to estimate the effects of RP on morbidity and non-drug health care expenditures of seniors who were already using the higher priced drugs targeted by RP when the policy was introduced. These seniors, all of whom were potentially affected or ‘exposed’ to RP, were compared to seniors who, prior to the introduction of RP, were using drugs that remained fully reimbursed under RP. We then estimated the pre-post RP changes in indicators of morbidity (hospital admissions for cardiovascular disease, and associated length of stay, hospital-based revascularization, prescriptions of sublingual nitroglycerin, physician hospital and emergency room consults, physician ambulatory consults, surgical and diagnostic physician services related to cardiovascular disease) and health care costs (physician and hospital-specific) of those seniors exposed to RP. The corresponding changes for beneficiaries not exposed to RP were used to control for secular trends. We distinguished between the short run vs long run effects of the RP policy. Shortrun effects occurred within the first 4 months of the implementation of the policy; long run effects occurred from the introduction of the policy to the end of the sample period, March 1998. This period was 29 months for nitrates users, and 15 months each for ACE inhibitor and CCB users.

While most subjects using an ACE inhibitor were not using CCBs, and similarly, most using CCBs were not using ACE inhibitors, there were 7,090 subjects using both ACE inhibitor and CCB drugs. A large proportion of the latter group (86% or 6,094 subjects) took either a Restricted ACE inhibitor or CCB, with 2,385 (34%) taking both Restricted ACE inhibitors and CCBs. These individuals were potentially affected by the application of RP to 2 of their medications at the same time, and could have endured the most deleterious impact of the policy. We removed those taking ACE inhibitors and CCBs concurrently and will investigate the health consequences of RP on these subjects in future research.

Using patient-level data, we estimated the effects of RP on death due to cardiovascular disease and time to admission to a longterm care facility. These were estimated using survival models in which we compared time to event for those exposed and not exposed to RP, while directly controlling for confounding variables, i.e., variables that are associated with both survival and RP exposure status. To ensure results were robust, we compared the survival differences between those exposed and not exposed to RP during the year *prior* to the introduction of RP. This quantity isolates the influence of confounding variables and was used to adjust the survival differences between those exposed and not exposed to RP during the year after the introduction of RP.

If RP adversely affects patient health status, then assessing the extent to which income improves access to Restricted drugs provides evidence about the equity of this policy. To obtain a Restricted drug after the introduction of RP, Pharmacare beneficiaries can either pay the additional charge or receive an exemption, in which case Pharmacare pays the additional charge. Using data on subjects who were using Restricted drugs prior to RP, and who survived at least 1 year after the introduction of RP, we modeled how senior's income status (an indicator of low income) affected both the probability of exemption from RP, and, in the subsample of seniors who were not exempted, both the probability of any payment and the amount paid for Restricted drugs. We used both linear and logit regression models to estimate the effect of low income status on these outcomes, while controlling for patient age at introduction of RP, sex, an indicator of low income, and morbidity, as measured by the use of prescription drugs, physician and hospital services in the 13 months prior to the introduction of RP. The same methods were used to model the effect of low income status on the probability of switching to an Unrestricted drug or substitute within 1 year of the introduction of RP.

Notes on the interpretation of the effects of RP on morbidity.

1. 'Exposure' to RP is defined by the use, before the introduction of the RP policy, of the higher priced drugs eventually targeted by RP. This is best described as an indicator of 'potential' exposure to RP: Not all of those using Restricted drugs prior to the introduction of the RP policy would have their drug use disrupted by RP; some would have been continually exempted from RP, others would have paid out of pocket and would have not changed their drug consumption. Still others might have switched to a fully subsidized drug without any adverse effects. Our models therefore estimate the average health effect among a variety of subjects who might differ in the way their health changed after the policy.
2. While it is possible that RP itself could adversely affect patient health, it is also possible that RP could lead to the discovery of health problems that existed prior to the introduction of the policy. Some of those using Restricted drugs pre-RP would have consulted their physicians post-RP to discuss their treatment options (i.e., switch drugs, change the dose, apply for a special authority exemption) and would possibly have met again to monitor progress on a new drug. These additional physician interactions could have revealed pre-existing health problems that otherwise would not have been discovered until later. Hence an association between RP and morbidity (as measured by the use of health services) might not necessarily indicate that RP 'causes' morbidity.
3. The introduction of RP can potentially affect outcomes in ways that we do not explicitly examine, and hence our study is a partial equilibrium analysis. In particular, to the extent that RP is successful in reducing public expenditures on prescription drugs, it might permit public drug insurers to insure more drugs or provide drug subsidies to more individuals [28;29]. We did not account for any such effects in our analyses.
4. We focus on the effects of the RP policy on those senior Pharmacare beneficiaries who, prior to the introduction of RP, were taking drugs whose reimbursement was eventually

restricted under RP. We refer to these individuals as the ‘prevalent’ cohort. The effects of RP on this group might differ from the effects of RP on the group we refer to as to ‘incident’ cohort – those senior Pharmacare beneficiaries who initiated use of nitrates, ACE inhibitors or CCBs, *after* the introduction of the policy. Both cohorts were potentially affected by RP, but in different ways: in the prevalent cohort, RP increased the charges of medications already being used, whereas those in the incident cohort made their initial choice of medication in light of the higher charges for Restricted drugs. Consider the individuals in each of the cohorts who neither received exemption from RP nor paid out of pocket to use a Restricted drug. Such individuals in the prevalent cohort switched their medications, whereas those in incident cohort did not switch – they simply started therapy on an Unrestricted drug or substitute. To the extent that Restricted drugs are superior to Unrestricted drugs and substitutes, individuals in both incident and prevalent cohorts who do not use Restricted as a result of RP are harmed by the policy. But those in prevalent cohort are at greater risk from any adverse events due to drug switching. Hence our estimates of the effect of RP on the prevalent cohort likely provide an upper bound on the adverse health events associated with the effect of the RP policy on the prevalent cohort.

5. The group of seniors that we examine in this study faced a sudden change in the reimbursement of the higher priced drugs that were targeted by RP. Successive generations of senior Pharmacare beneficiaries may or may not face the same surprise. This depends on the age that individuals commence therapy for the drugs targeted by RP, and their level of anticipation of the policy. Individuals who are already eligible for senior (age 65+ years) Pharmacare benefits when initiating therapy, will make their initial choice of medication with knowledge of the higher charges for Restricted drugs. Those who initiate drug therapy while under age 65, and ineligible for Pharmacare benefits, might very well anticipate their upcoming eligibility for Pharmacare benefits, and elect to start on a Unrestricted drug. Alternatively, those who anticipate the RP restrictions might purchase supplemental drug insurance prior to reaching age 65, so that they face no additional charges irrespective of their choice of medication.

4 PROJECT RESULTS

4.1.1 Drug costs and use

We estimate that RP of the nitrates, ACE inhibitors and CCBs drug classes reduced Pharmacare expenditures on its seniors drug plan between \$23.8 to \$24.8 million (depending on the estimation method used) between October 1995 to May 1999. This translates into annualized savings to Pharmacare of about \$7.7 million, or 3.6% of the \$213.7 million that Pharmacare spent on drugs for seniors (not including dispensing fees) in 1997. The estimate of the effect of the introduction of RP on savings on the CCB drugs includes the savings attributable to the concurrent introduction of the policy which limited reimbursement of the sustained release versions of verapamil and diltiazem to the equivalent dosage strengths of the regular release versions. The net savings estimate was largely insensitive to the choice of estimation method. Approximately 24% (\$5.8 million) of Pharmacare's total savings represent additional costs to seniors who elected to pay for the higher cost drugs.

Most of the total savings are attributable to savings in the nitrates and CCB drug classes; savings on ACE inhibitors were surprisingly low. This may have been due to the process by which the reference price for the ACE inhibitor drug class was set. Pharmacare limited reimbursement for the Restricted ACE inhibitors to a fixed amount, initially \$27, per 30 day supply. Seniors who used sufficiently low doses of the Restricted drugs such that the cost per 30 days was under this amount would have had the entire drug ingredient cost subsidized by Pharmacare. We found that, in the quarter in which RP was introduced, 46% of senior users of enalapril, a commonly prescribed Restricted ACE inhibitor, had monthly drug costs under \$27. Another potential explanation for the relatively low savings on the ACE inhibitors was that rates of exemption from the policy might have been especially high. About 50% of the seniors exposed to the RP of the ACE inhibitors had all of their post-RP Restricted drugs completely paid for by Pharmacare. The corresponding figure for nitrates users was 16%. Another, possibly related, reason for the relatively large savings associated with the introduction of RP for nitrates is that manufacturers voluntarily lowered retail prices of one of the most commonly prescribed nitrates, the nitroglycerin patch. After the price reduction, Pharmacare no longer applied to RP to the patch. The price reduction had the effect of guaranteeing a lower cost to Pharmacare for every patch dispensed. Had the manufacturers not lowered prices and had RP still been applied, then subsequent savings would have depended on the number of patient exemption requests from physicians.

It should be noted that the estimates of the effect of RP on Pharmacare expenditures for its senior beneficiaries do not include any savings Pharmacare realized from the application of RP to its other beneficiary groups, including welfare recipients and households with large drug costs relative to income. While these other groups constitute about 50% of all Pharmacare beneficiaries, because they likely have lower rates of use of the cardiovascular drugs targeted by RP, savings from RP to the cardiac drugs are likely lower. For example, based on Pharmacare data for the years 1998 and 1999, 8 of the top 10 drugs dispensed to seniors, ranked by total Pharmacare expenditures, were used for the management of cardiovascular disease. By contrast, none of the top 10 drugs dispensed to welfare recipients, who constitute the second largest

beneficiary group, were used for cardiovascular disease.³ The drug cost savings estimates also do not include any savings that Pharmacare realized from the application of RP to the nonsteroidal anti-inflammatory drugs, or the concurrent application of RP and the closely related Special Authority program to the H2-blockers and the proton pump inhibitors (PPIs), respectively.⁴

After the introduction of RP, there were sharp changes in the prescribing of the individual drugs within each of the 3 drug classes. Within 3 months of the implementation of nitrates RP in November 1995, the use of the reference standard nitrate products increased 177% over baseline values. There was a corresponding 65% decline in the use of the oral Restricted nitrates. The use of the nitroglycerin patch initially dropped 32%, but after Pharmacare no longer restricted its reimbursement of the patch, use eventually increased by 55% over its pre-RP levels.

After RP was applied to the ACE inhibitors, both the level and rate of growth in the use of the Restricted ACE inhibitors (enalapril in particular) fell, whereas the use of the Unrestricted ACE inhibitors (in particular ramipril and to a lesser extent quinapril) grew sharply, and more than compensated for lower use of the Restricted ACE inhibitors. In fact use of all types of ACE inhibitors grew 50% per capita from the baseline period (October 1995 - September 1996) to the period April 1998 - May 1999.

Dispensing of felodipine, the reference standard CCB, increased by 111% of its pre-RP levels within 29 months after the introduction of RP. There was only a 7% drop in the use of the Restricted CCBs, over the same time period. The reason for this small decline was due to increased use of the Restricted drug amlodipine, which offset reductions in the use of sustained release nifedipine.

4.1.2 Mortality

We could not reject, at the 5% significance level, the hypothesis that mortality rates associated with cardiovascular or renal disorders were higher for subjects who were exposed to the RP of nitrates, ACE inhibitors or CCBs. We obtained this result using both of the methods used to estimate the effect of RP on mortality.

4.1.3 Morbidity and physician costs

We could not reject, at the 5% significance level, the hypothesis that longterm care admission rates were higher for subjects who were exposed to the RP of nitrates, ACE inhibitors or CCBs. We obtained this result using both of the methods used to estimate the effect of RP on the likelihood of longterm care admission.

The use and expenditures on ambulatory physician consultations increased after the implementation of the policy, likely due to the fact that many seniors needed to consult with their

³ See: <http://www.moh.hnet.bc.ca/pharme/outgoing/PcareTrends2000.pdf>

⁴ Preliminary estimates from related research in progress suggest that the programs targeting the H2 blockers and PPI drugs reduced Pharmacare expenditures by approximately \$7.3 million annually, almost as much as the annualized savings attributable to the application of RP to the cardiac drugs.

physicians to discuss treatment options (e.g. switch to a fully subsidized drug, apply for an exemption), and to monitor the progress of those who switched drugs. The increased visits could have been due to changes in patient morbidity as well. The longrun physician consultation rates for ACE inhibitor users increased 11% after the introduction of RP; the corresponding figure for CCB users was 7%. Among nitrate users, additional visits were concentrated in the first 4 months of the policy; visits increased by 9%, but this was offset by a subsequent reduction in visits. We found that those exposed to ACE inhibitors RP (i.e. those taking Restricted ACE inhibitors prior to the introduction of the policy) incurred an additional \$0.65 per month (95% CI: \$0.38 to \$0.93) in the longrun, and those exposed to CCBs RP incurred an additional \$0.40 per month (95% CI: \$0.17 to \$0.62) in the longrun. These figures were multiplied by the number of exposed in our sample, and multiplied again by their respective exposure periods. We estimated that the total additional consultation costs associated with the introduction of RP to 28,234 users of Restricted ACE inhibitors and 14,234 users of Restricted CCBs over the 15 months following the policy introduction was \$308,000 and \$110,000 respectively.

These are likely conservative estimates of the cost of additional physician consultations: unlike our analysis of the effects of RP on drug costs, in which we used data on all Pharmacare senior beneficiaries, the analysis of physician services costs was based on the subsample of seniors for whom we could ascertain their RP exposure status. There are subjects who we did not use in our analyses who may have consulted with physicians to discuss post-RP treatment options and the cost of these additional consultations are not included. In particular, our sample inclusion criteria required that the subject be taking a nitrate, ACE inhibitor or CCB for at least 19 of the 20 week period ending with the announcement of RP. Individuals who were hospitalized for several weeks during this period, or used these drugs intermittently likely would not be included in our sample. Had double the number of subjects actually been affected by RP, costs of additional physician consults may have been as high as \$850,000.

Sublingual nitroglycerin is taken to manage acute exacerbations of angina. We used the prescription of this drug as an indicator of morbidity. We detected a shortrun increase in the proportion of nitrates users who were dispensed sublingual nitroglycerin in the 4 months after the introduction of RP. Specifically, the odds of being dispensed the drug were 18% higher for those exposed to RP. No effects were observed on the mean number of sublingual nitroglycerin prescriptions dispensed among exposed nitrates users. No effects were detected among ACE inhibitor or CCB users.

We also found a long run increase in the likelihood of both a hospital-based revascularization procedure and a physician CVD related surgical procedure for those exposed to the nitrates RP policy. And these effects were relatively large: we estimate that the longrun odds of revascularization increased after exposure to RP by between 6-7 times. There were no long run effects of RP on the morbidity of those exposed to the ACE inhibitors or CCB RP policies, although there were some short run increases in revascularizations and related physician surgical procedures for those exposed to the ACE inhibitor RP policy.

The estimates of the effect of RP on morbidity should be interpreted with some caution: While we found that those exposed to nitrates RP policy had a higher likelihood of revascularization, and related physician services, there was no evidence of increases in probability or mean number

of CVD-related hospital admissions or associated length of stay. And surprisingly, our models suggest that those exposed to the RP of CCBs had *fewer* admissions and shorter stays. In some cases, formal tests cast suspicion on the adequacy of our research design: Results of the models of the effects of ACE inhibitor RP on CVD-related hospital admissions and associated length of stay were simply discarded because the pre-RP trend in these variables for the exposed were statistically different from the trends observed for the comparators. The same was true for the models of the effect of CCB RP on physician hospital and emergency room consults. Hence for some models, no evaluative evidence on the impacts of RP are available.

In future research we will examine the robustness of the evidence of the effect of RP on morbidity. First, instead of estimating the short run and long run effects of RP on outcomes using two indicator variables, we will estimate the effect of RP using month-specific indicator variables for each of the months after the introduction of RP. Second, we will pay closer attention to the appropriateness of the use of the trends in the morbidity outcomes of the Unrestricted drug users to estimate the trends for the Restricted drug users, had they not been exposed to RP. One such approach is similar to the replication strategy used for the analysis of the effects of RP on mortality. We could repeat the analysis, this time redefining the exposed and non-exposed groups based on their use of Restricted and Unrestricted drugs 1 year *prior* to the introduction of RP. The difference in the subsequent 1 year trends between these 2 groups could be used to assess the biases introduced by using Unrestricted drug users as comparators.

Given the uncertainty regarding the adequacy of the specification and estimation of the morbidity models based on the use of physician and hospital-based services, we postponed estimation of the effects of RP on the costs of associated physicians' and hospitals services.

4.1.4 Effect of income on access to the partially subsidized 'Restricted' drugs

We found that among those using ACE inhibitors or CCBs, those with low income have the same probability of exemption as do those with high income. Among nitrates users, those with low income are at least 2% more likely to be exempted than those with high income. Among the subsample of those not exempted from RP, low income status has some effect of the probability and amount paid. Those with low income are between at least 4-5% less likely to pay more than \$1 for Restricted drugs over the year following the introduction of RP. Of those that do pay more than \$1, low income seniors pay between at least \$6.48 to \$10.88 less than do higher income seniors. These represent proportional reductions of between at least 6%-14%, depending on the drug class (12% for nitrates, 6% for ACE inhibitors, 14% for CCBs). The interpretation of these figures is that low income seniors who do not receive continuous exemptions from RP use slightly fewer Restricted drugs post policy and hence are more likely to switch to a fully subsidized drug, or reduce or discontinue drug use. Hence for those seniors who are not exempted from RP, there is some evidence of income-based impediments to access for the Restricted drugs, although the impediments do not appear to be particularly large. This was confirmed by estimates of the effect of low income status on the probability of switching to an Unrestricted drug or substitute, among those using Restricted drugs pre-RP. Low income Restricted nitrates users had a 1.7% higher probability of switching within a year of the policy introduction; the corresponding probability for ACE inhibitors was 1.3% and for CCBs, no effects were found.

4.1.5 Is Reference Pricing worth it?

From the perspective of the BC Ministry of Health, a comprehensive assessment of the RP policy requires quantification of all of its costs and benefits. This study estimates the benefits but not all of the costs of the introduction of the RP policy to senior Pharmacare beneficiaries. On the benefits side, we estimate that the application of RP to the nitrates, ACE inhibitor and CCB drugs was associated with a reduction in expenditures on its seniors drug plan in the order of \$24 million as of May 1999. On the other side of the ledger are the additional expenditures on ambulatory physician consultations (likely under \$1 million), and the costs of the additional revascularization procedures, and the cost of the additional sublingual nitroglycerin dispensed to nitrates users. We have not yet estimated all of these costs because of uncertainty as to the validity of our models. A full assessment would also need to incorporate the variable costs of administration of the RP program (the additional staff required to handle exemption requests, for example). Until these costs can be quantified, statements regarding the overall effects of RP are premature.

5 DISSEMINATION PLAN

The dissemination strategy for this project is multi-faceted to address the needs of a number of audiences:

1. A specific policy Summary Report will be developed for managers and policy-makers that will present the results and conclusions of this project and its relationship to the existing literature. A professional communications consultant will be hired to assist with publication of the Summary Report. Copies of the Report will be sent to all executive directors of the Provincial/Territorial Drug Plans.
2. Grootendorst will make presentations directly to executive at the Ontario Drug Benefit program.
3. Other stakeholders will be apprised of the results using the Research Transfer Program of the McMaster University Centre for Health Economics and Policy Analysis (CHEPA). Under the Program, our findings will be summarized and “translated” into lay language by a professional medical journalist and mailed to over 1,500 regular subscribers including policy makers, academic researchers, and other stakeholders.
4. Traditional means of research dissemination will also be used. Two articles will be submitted for publication in academic journals, one dealing primarily with the policy implications of the findings and the other dealing with methodological issues. The former manuscript will be submitted for publication in an academic health policy journal (e.g. *Canadian Public Policy*). The latter manuscript will be submitted for publication in an academic health economics, or health services research journal (e.g. *Journal of Health Economics*, *Health Economics* or *Medical Care*). Abstracts of the research will be submitted for presentation at various academic conferences (e.g. the upcoming Canadian Health Economics Research Association conference in Halifax in May 2002).
5. Preliminary results have already been presented to seminar participants at the 2001 International Health Economics Association meetings, York, UK; 2001 Canadian Health Research Association meetings, Toronto; Ontario Ministry of Health, Toronto; Department of Economics, York University, North York; the Institute for Clinical Evaluative Sciences, Sunnybrook Hospital, Toronto; Centre for Evaluation of Medicines, St. Joseph's Hospital, Hamilton; and the Harvard School of Public Health, Harvard University.

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Health Transitions Fund Project Summary NA222:

HTF Project Title:

The impact of reference pricing of cardiovascular drugs on health care costs and health outcomes: evidence from British Columbia

Topic:

We estimate the effects of Reference Pricing, a drug cost control policy introduced by the BC Ministry of Health Pharmacare program in 1995, on its program expenditures for seniors, out of pocket costs paid by its senior beneficiaries, indicators of beneficiary health status and attendant Ministry of Health expenditures on physicians and hospitals services.

Sponsor Organizations:

Father Sean O'Sullivan Research Centre, St. Joseph's Hospital, Canadian Health Services Research Foundation; Brogan Inc.; BC Ministry of Health; Drug Information Association.

Rationale:

Reference pricing (RP) limits the reimbursement of a group of drugs with similar therapeutic effect but different active ingredients to a fixed 'reference price'. The setting of the reference price varies by jurisdiction but typically is based on an average of the lowest cost 'reference standard' drugs within the group. Critics of RP contend that the partially subsidized and fully subsidized (reference standard) drugs are not therapeutically interchangeable, and therefore patient health will be compromised and use of other non-pharmacologic health services may increase as a result, thus partially or wholly offsetting any potential cost savings from the policy.

Key findings:

The application of RP to 3 groups of cardiac drugs produced annualized savings to Pharmacare of about \$7.7 million, or 3.6% of the \$213.7 million that Pharmacare spent on drugs for seniors (not including dispensing fees) in 1997. We found that the additional costs for physician consultations to be modest, around \$500,000 in the subsample of seniors we studied, from the introduction of the RP plans to March 1998, although the costs could be greater, perhaps up to twice this amount, if we accounted for all seniors exposed to the RP over the same period. We found no effects of RP on mortality, or premature admission to a longterm care facility. Seniors using the nitrate drugs for angina that were no longer fully subsidized when RP was introduced faced a higher probability in the short run of using medicines to deal with acute exacerbations of angina and in the longer run having bypass surgery or other revascularization procedures. No long run effects of morbidity were observed for the application of RP to two different types of anti-hypertensive medications, although there was an short run increase in the rate of revascularizations among those taking 1 type of anti-hypertensive: the ACE inhibitors. The results of these morbidity models should be seen as tentative, until these results can be replicated using alternative estimation strategies.

Policy Implications:

The introduction of RP can indeed reduce Ministry of Health drug expenditures. The effects of RP on patient morbidity remain to be fully investigated before policy recommendations can be offered.

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