Pharmaceuticals: Therapeutic Interchange and Pricing Policies

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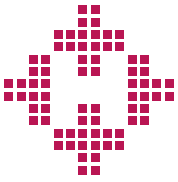

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We thank the University of Manitoba, Faculty of Medicine, Health Research Ethics Board for their review of this project. The Manitoba Centre for Health Policy complies with all legislative acts and regulations governing the protection and use of sensitive information. We implement strict policies and procedures to protect the privacy and security of anonymized data used to produce this report and we keep the provincial Health Information Privacy Committee informed of all work undertaken for Manitoba Health.

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Executive Summary

Due to the high costs of drug research and development and the public stake in purchasing pharmaceutical products, the competing policy objectives of securing low prices for pharmaceutical products and encouraging valued innovation create considerable tension in the pharmaceutical sector (Jacobzone, 2000; Willison et al., 2001). Patients and health care managers want low prices for pharmaceutical products on the one hand, and rapid development of new treatments on the other. These two goals may not be as contradictory as they appear. Fostering a climate of competition between patented and non-patented drug products may lower pharmaceutical costs while providing appropriate incentive for research of greatest social value. This is because cost-effective drug use ensures that manufacturers will be rewarded for the therapeutic value-for-money their products provide relative to competing alternatives. When consumers and prescribers become more cost-conscious, and consider the relative costs and benefits of alternative treatment options, the incentive for expensive and duplicative "me-too" product innovation is reduced. When premium prices are paid only for those products that generate true value-for-money, the market stimulates search for only such therapeutic breakthroughs.

This project focuses on policies that would improve the competitiveness of pricing and the cost-effectiveness of product selection in a specific subset of pharmaceutical products. We investigate therapeutic interchange policies and alternative mechanisms to reduce both the public and private cost per episode of care with angiotensin converting enzyme inhibitors (henceforth, ACEIs) and/or angiotensin II receptor antagonists (henceforth, A2RAs). These related therapeutic classes of drugs are commonly used to treat hypertension and other cardiovascular risks. Rapidly increasing in use, these products accounted for 5.5% of total prescriptions and 8.2% of total prescription drug expenditures in 1999/2000 (Metge et al., 2003).

According to economic theory, the similarities among patented and generic products within the ACEI category should lead to intense price competition, producing significant value at low-cost for consumers. Similarly, given the general similarities of the products in both the ACEI and A2RA classes, economic theory would predict that the use of A2RA drugs would be reserved for only those patients who have tried and failed on ACEI drugs or that the manufacturers of A2RA drugs would charge prices that are competitive vis-à-vis ACEI products. These predictions would likely be accurate if ACEI and A2RA products were like ordinary goods, and if patients were ordinary consumers. In truth, pharmaceuticals are different. And the patterns of consumer use and firm pricing behaviour in the pharmaceutical

marketplace are not always as they would be elsewhere. This study indicates that firms are less than perfectly competitive and that consumer cost-sensitivity is low.

For the purpose of these analyses we assume that the initial decision to prescribe either ACEI or A2RA therapy is appropriate. Moving forward from this assumption, we model the impact of policies that would endeavour to manage prices and product choices within these therapeutic classes. Specifically, we investigate the impact on both public and private drug expenditures of (1) pricing policies as they pertain to the relative cost of generic drugs (vis-à-vis brand name equivalents), (2) therapeutic interchange policies for the ACEI subclass, and (3) a step-up protocol for managing utilization of A2RAs.

Over the period of study, 1998/99 to 2000/01, there were over 16 different types of products (grouped by active ingredients) that could be prescribed to patients from the A2RA and ACEI drug categories—six types of A2RA drug and 10 ACEI drug types. The analysis of market dynamics within the ACEI class revealed little evidence of price competition between brand and generic non-patented products. In some cases, brand name products achieved a majority of market share despite the presence of generic competitors. This might not be surprising given that generic competitors were not priced at a significant discount relative to the brand. The price of few of the generics in these market segments seldom fell below 80% of the price of their brand name competitors. Generic versions of captopril and lisinopril offered virtually no discount over corresponding brands. Furthermore, in eight of twelve comparisons made between prices paid for generics in Manitoba and other provinces, prices in Manitoba were (from 7 to 9%) higher than elsewhere in Canada. In only three comparisons were Manitoba prices lower (3%).

Utilization patterns involving A2RA drugs indicated inefficiencies in product selection. These relatively newer products were not being reserved for only those patients who have tried and failed on ACEI drugs. Growth in expenditures on A2RA drugs far exceeded the growth in expenditures on ACEI products. The share of the annual ACEI and A2RA drug market segment accounted for by A2RA drug products grew from 13 to 22% in the two years between 1998/90 and 2000/01. Much of the growth in A2RA expenditures was due to increased purchases by new users of the products that had not previously tried an ACEI drug.

To illustrate the potential to achieve competitive pricing among patented and non-patented drug products, together with cost-conscious product selection by patients/prescribers, we simulated multiple stages of policy intervention for the ACEI and A2RA drug classes. Each of these policy simulations builds in logical sequence, starting with policies that promote

generic price discounts and generic substitution. Onto this baseline, "therapeutic interchange" policies are added—reimbursing consumers at the rate of the lowest price equivalent drug—a policy that would promote consumers' price sensitivity when selecting among both patented and non-patented products. Finally, a "step-up" policy to encourage first-line use of ACEI products is added to these simulations.

The results of this analysis illustrate that generic pricing and substitution policies are a necessary first step if Manitoba is to realize the potential benefits of improved pricing and product selection in these classes. Generic substitution policies on their own produce between $1.5 and $2 million in savings within the ACEI category of drugs alone, representing over 10% of total spending in this class. (All savings estimates are the total of public and private savings that may be realized.) Combining generic substitution and negotiated generic price cuts through a tendering process may be an attractive policy option insofar as it can produce savings through cooperation with manufacturers.

After generic pricing policies have secured competition between competing versions of non-patented drugs, policymakers might consider "therapeutic interchange" and "step-up" programs. Therapeutic interchange policies for ACEI drug products could generate as much as $5 to $7 million in annual savings in Manitoba. A step-up policy requiring that ACEI products be tried prior to the use of A2RA drugs could generate an additional $250,000 or more in savings. Though the "savings" generated by the step-up policy appear small, its implementation might be necessary if a therapeutic interchange policy is to be used on ACEI drug products. The step-up policy would avoid the potential side effect that a therapeutic interchange policy on ACEI products may promote the first-line prescribing of A2RA drugs.

The potential savings generated by therapeutic interchange policies or prescribing protocols must be weighed against their potential to provoke negative response from manufactures and prescribers. Therapeutic interchange, in the form of reference-based pricing, provoked a considerable backlash from drug manufacturers in British Columbia. The industry's threat to reduce investment in the province was sufficient ground for the government to put all plans of expanding their program on hold.

1.0 INTRODUCTION

At $15 billion per year, pharmaceuticals are second to hospitals in terms of Canadian health care spending. But they are first in terms of expenditure growth. Prescription drugs have been the fastest growing component of Canadian health expenditures for many years. Growing pharmaceutical costs create pressures both on and for public pharmacare programs. Drug expenditure inflation motivates calls for increased public drug subsidy for individuals facing high drug bills. Growing drug costs also constitute a sustainability threat to programs that currently offer such subsidy. Ensuring that Canadians receive value for money spent on pharmaceutical care may relieve pressure on both fronts.

ACEIs and A2RAs are a therapeutic class of drugs commonly used to treat hypertension and other cardiovascular illnesses. These products account for 8.2% of total prescription drug expenditures in 1999/2000.

This project focuses on policies that would improve the competitiveness of pricing and the cost-effectiveness of product selection in a specific subset of pharmaceutical products. We investigate therapeutic interchange policies and alternative mechanisms to reduce both the public and private cost per episode of care with angiotensin converting enzyme inhibitors (henceforth, ACEIs) and/or angiotensin II receptor antagonists (henceforth, A2RAs). These related therapeutic classes of drugs are commonly used to treat hypertension and other cardiovascular risks. Rapidly increasing in use, these products accounted for 5.5% of total prescriptions and 8.2% of total prescription drug expenditures in 1999/2000 (Metge et al., 2003).

This study focuses on policies that improve pricing of these drug products but does not relate this to other therapeutic categories of drugs.

For the purpose of these analyses we assume that the initial decision to prescribe either ACEI or A2RA therapy is appropriate. Specifically, we assume that patients have been accurately diagnosed with conditions for which ACEIs and A2RAs are indicated, and that the best available evidence indicates that an ACEI or an A2RA drug would be a cost-effective therapeutic option for patients receiving ACEIs or A2RAs. We do not assume, however, that patients are necessarily receiving the most cost-effective drug from within the ACEI or A2RA drug categories. Put another way, the policy options explored here are to improve the competitiveness of pricing and the cost-effectiveness of product selection within the ACEI or A2RA drug categories but do not consider the competitiveness of pricing or the cost-effectiveness of product selection vis-à-vis other therapeutic categories.

Moving forward from this assumption, we model the impact of policies that would endeavour to manage prices and product choices within these therapeutic classes. Specifically, we investigate the impact on both public and private drug expenditures of (1) pricing policies as they pertain to the relative cost of generic drugs (vis-à-vis brand name equivalents), (2) therapeutic interchange policies for the ACEI subclass, and (3) a step-up protocol for managing utilization of A2RAs.

1.1 Balancing Health and Industrial Policy

Lower pharmaceutical pricing may actually foster efficiency in the innovation process.

Competing policy objectives of securing low prices for pharmaceutical products and encouraging valued innovation create considerable tension in the pharmaceutical sector due to the high costs of drug research and development and the public stake in purchasing pharmaceutical products (Jacobzone, 2000; Willison et al., 2001). The tension between "health care innovation" and "health system efficiency" may be more apparent than real. The economics of innovation and patents points to the potential that lower pharmaceutical prices may actually foster efficiency in the innovation process.

"Information can be expensive to produce, inexpensive to reproduce, and difficult to profit from." Discovering new ideas or processes can take a lot of time, talent, energy, and resources—and often, a little luck. These costs of the search process are "sunk" in economic terms; in contrast to tangible investments that can be sold, traded, recycled, or reused, research activity can seldom be "retrieved" in any real sense. Firms cannot "get back" the time, money, and energy spent investigating an idea. Furthermore, if a firm is lucky enough to make a discovery, the intellectual asset generated is very inexpensive to reproduce. Information is very easy to reproduce. The often high sunk costs of innovation combined with the low-costs of duplication can generate a market failure.

Incentive to invest in the research activities necessary to bring new ideas to market is reduced by the potential for duplication and competition.

If innovators were subject to direct competition, competing firms could copy their technologies and bid prices down to marginal cost—the point where firms are just covering the cost of production and distribution. The innovator would be unable to recoup the sunk costs of the innovative process when the end product is sold at competitive prices. Consequently, the potential for duplication and competition reduces the incentive to invest in research activities necessary to bring ideas to market in the first place. This is an undesirable outcome if both consumers and producers can somehow be made better off through a process that balances the need to reward innovation while fostering competition in end-markets.

Patents are one means of protecting the intangible asset generated through research processes. A patent creates a temporary, state-conferred monopoly over the sale of a product by prohibiting the unlicensed entry of competitors. Its purpose is to provide incentive for firms to invest resources in the innovative process, while balancing the want for innovation against the desire for efficiencies created through competition.

Patents may be viewed as forward-looking policy tools that are based largely on market principles. They are forward-looking insofar as the reward for research is not based on the cost of research but on the value of the innova-

tion product brought to market. They are market-based insofar as rewards are determined by the market's valuation of the innovative outcomes. Research grants and tax subsidies for research, by contrast, are examples of policies that relate directly to the cost of the research endeavour, not to the value of its output.

Because patents provide incentive based on market value to end-users, there is no guarantee that investment costs will be recouped. If a patented product is of little value, the market may not support sufficient sales at a sufficient mark-up to cover the cost of the research expenditure needed to bring the product to market. This should not be a concern to policy-makers. Firms that gamble with research investment sometimes lose. On the other hand, there is also no guarantee that a patentee will only charge a price that reflects average costs if the market will support a much higher price. Patentees may earn large profits. This too should not be a concern—firms that gamble sometimes win.

Are drugs over- or under-rewarded in the pharmaceutical marketplace? Policy-makers need to determine whether the market's value on patient pharmaceuticals provide firms with incentive to research.

What should be of concern to policy makers is determining whether the market's valuation of patented discoveries provides incentive for research of the greatest value to society as a whole. Are drugs over- or under-rewarded in the pharmaceutical marketplace?

Unlike conventional marketplaces, efficiency of product selection decisions and competitiveness of firm pricing policies cannot simply be assumed in the pharmaceutical marketplace. In the pharmaceutical sector, it may be inappropriate to assume that decision-making always results in choices where the quantity or quality of derived health outcomes is proportional to the cost of prescribed drug products. Asymmetric information, imperfect decision-making, and non-standard financial incentives are all common in the pharmaceutical sector, and all inconsistent with the model of consumer behaviour that guarantees a relationship between the relative price and the relative value of goods purchased (Berndt et al., 2000). Further, the pharmaceutical market has limited capacity to support the large numbers of competing firms necessary to ensure that off-patented products are competitively priced. The number of firms that can be supported in this sector is naturally limited by economies of scale in research and manufacturing, by the fixed costs of product approval, and by inventory costs associated with carrying multiple product lines that, in the case of generic competitors, are identical in therapeutic terms. As a function of the unique features of the pharmaceutical marketplace, it is possible that both patented and non-patented drugs achieve sales at prices that could be considered excessive from the perspective of balancing health innovation policies.

Despite the importance of economies of scale and other supply-side limitations to competition in this sector, it is arguable that the unique constella-

The "moral hazard" (the tendency to overspend when it is not one's own money one is spending) influences both patients—who have full insurance coverage for pharmaceuticals—and prescribers who are almost never financially accountable for decisions made.

tion of incentives and information of decision-makers on the demand-side in the sector is the primary reason that purchases may take place at prices exceeding value (Evans, 1984; Morgan, 2000). Patients, who seek alleviation of pain, illness or risk thereof, are often fully insured against the cost of treatment options, giving rise to the possibility of "moral hazard" (the tendency to overspend when it is not one's own money one is spending) (Pauly, 1983; Coulson and Stuart, 1995). At the same time, patients have limited capacity to access and rationally process the complex information required to efficiently chose among treatment options. Prescribers, who have been delegated decision-making authority over treatment options, are almost never financially accountable for decisions made, giving rise to another form of "moral hazard"; they seldom possess accurate knowledge about the cost of alternative products (Miller and Blum, 1993; Barclay et al., 1995); and they have pressing time constraints that limit the extent to which they can seek independent information about the balance of risks, benefits, and costs of alternative medicines (Tamblyn and Perreault, 1998; Wazana, 2000).

In order to stimulate the search for therapeutic breakthroughs and steer the research sector away from developing duplicative "me-too" innovations, a climate of competitive pricing is required.

In the current context, demand-side decision-making in the pharmaceutical sector can lead to excessive utilization or the selection of more costly products when lower cost alternatives would be more cost-effective. This can generate financial reward for "discoveries" that are imitative; that is, the system can provide as much return on investment (or more) in the search for patentable imitation products as it does for discoveries that are truly innovative. Fostering a climate of competitive pricing between and among patented and non-patented drug products may lower pharmaceutical costs in a manner that reduces the incentive for duplicative, "me-too" innovations while continuing to stimulate the search for therapeutic breakthroughs. As has been noted in the past, creating a more efficient marketplace today will help steer the research sector away from searching for yet another me-too product within already crowded therapeutic classes toward more challenging but potentially more rewarding research endeavours (Canada, 1985).

1.2 Setting a Fair Price

One dimension to providing appropriate reward for innovation, and therefore incentive for research and development, is the payment of a fair price. In Canada, price regulation is fragmented along federal/provincial lines. The federal government plays a role in establishing the maximum for patented drug manufactures' factory-gate prices through the Patented Medicine Prices Review Board (PMPRB). Provincial governments, charged with containing the costs of public drug programs, can influence the retail cost of patented and non-patented medicines (inclusive of wholesale and retail mark-ups).

As the largest purchasers of pharmaceutical products in Canada, provincial governments' purchasing power may be sufficient to counter some of the

supply-side power of drug manufactures. Price regulating policies in most provinces focus on formulary listing decisions—the consideration of manufacturers' applications to list drugs on a formulary—and on pharmacy reimbursement policy.

Mechanisms used to reimburse pharmacies for products dispensed can influence drug prices by altering mark-ups in the distribution chain, by providing incentive for firms to "match" set prices, or both. Commonly used drug reimbursement policies include "Maximum Allowable Cost" pricing and "Actual Acquisition Cost." Actual Acquisition Cost reimbursement pays retailers an amount equal to their acquisition cost plus a pre-negotiated mark-up. The accuracy of reported acquisition costs may be regulated by ongoing monitoring or by the threat of random audit. Maximum Allowable Cost prices are published list prices that define the maximum contribution of a drug plan to the purchase of a drug. These policies may or may not prohibit retailers from adding extra patient charges on top of the reimbursed price.

Provincial governments are the largest purchasers of pharmaceutical products in Canada. Ontario and Quebec have the potential to have the most impact on pricing, due to the large volumes of pharmaceuticals purchased.

Saskatchewan, British Columbia, Alberta, and Nova Scotia use Actual Acquisition Cost to determine reimbursement rates (CPhA, 2002). Saskatchewan, for example, uses Actual Acquisition Cost to determine reimbursement rates for all products (CPhA, 2002). The cost used is the lesser of the pharmacy's actual cost of acquisition—including all rebates received by the provider except those for prompt payment of invoices—or the acquisition cost established by the government tendering process.

Manitoba, Ontario, Quebec, New Brunswick, Prince Edward Island, and Newfoundland and Labrador all use list prices to determine reimbursement (CPhA, 2002). In Manitoba, the reimbursed cost for products for drugs listed in the Manitoba Drug Interchangeability Formulary is the lowest normal price for the smallest available quantity as quoted by selected wholesalers (CPhA, 2002). For personal care home providers Manitoba uses Actual Acquisition Cost (AAC) to determine reimbursement rates.

Ontario and Quebec use list prices that have been negotiated with suppliers. Owing to their large size, the negotiations in Ontario and Quebec may have a substantial impact on pricing in other provinces.

Ontario reimburses pharmacies for drugs covered under the Ontario Drug Benefit Formulary at the "Drug Benefit Price." Since 1994, the Ontario government has frozen all existing Drug Benefit Prices—effectively limiting the year-over-year changes in drug prices to zero. Prices for new single source products are determined in letters of agreement between the manufacturer and the drug plan. Intended to set out price-volume forecast that give budgetary predictability and negotiation leverage, these agreements

achieve low "list" prices. Finally, Ontario requires entrants into multi-source product categories to be priced at discounts over incumbents—the first entrant must be priced 30% below the brand name product and successive entrants must be priced 10% below that benchmark.

Since 1993, Quebec has reimbursed pharmacies based on the manufacturer's guaranteed selling price plus mark-ups. The guaranteed selling prices are required to equal the lowest prices charged to any other purchaser in Canada. This policy secures the best available price for Quebec; however, its side effect is that it limits the scope for price negotiation in smaller provinces. Any discount given to a small province must also be given to Quebec. This appears to have limited price discounts attained in small provinces that previously had engaged in aggressive negotiations, most notably Saskatchewan (FPT TFPP, 1999; Morgan et al., 2003).

There is remarkable harmony of drug prices in Canada. However, Manitobans pay the highest prices for generic drugs in Canada.

Despite variety in reimbursement mechanism, there is remarkable harmony of drug prices in Canada. Possibly owing to the levelling effect of guaranteed selling prices in Quebec, researchers have found that there is less than a 10% variation across provinces in the average of prices charged for the 101 top-selling pharmaceuticals in Canada (Morgan et al., 2003). There is, however, wider variation in the relative price of generic suppliers in Canada. Research has shown that Manitoba has the highest prices for generic drugs (relative to their brand name counterparts) in Canada (FPT TFPP, 1999; PMPRB, 2002).

1.3 Managing Intra-class Prices and Utilization

Recent studies have shown increased utilization of drug therapy and increases in the cost of drug therapy have contributed about equally to growing expenditures (Merlis, 2000; Morgan, 2001b, 2002; PMPRB, 2002). Increased utilization is measured by the number of drug units consumed (pills, tablets, etc.), the number of prescriptions received, or the number of some standardized measure of duration of treatment (days supplied, defined daily doses, or episodes of treatment). Increases in the cost of therapy are a function of changes in the price of drugs sold and changes in the mix of drugs selected per treatment.

Newer medicines are typically more expensive than older, off-patent medicines. This has a substantial impact on the cost of health care.

The changing mix of drugs used for pharmaceutical treatment can have a substantial impact on the cost of health care because newer medicines are typically more expensive than older, off-patent medicines (Morgan, 2001b). Inflation caused by product substitutions should not be a concern when price differences between new and old products are balanced by proportionate differences in the quality of therapeutic outcomes. In some cases, however, new products launched into established therapeutic classes offer incremental benefits that do not justify the combination of high price and wide-

spread use. Related benefits—such as increased tolerability—often justify the cost of newer products only for specific subpopulations of patient, or when existing products have proven unsatisfactory.

Promotional materials—television ads, manufacturer sponsored medical education events—are the primary educators of patients and physicians about new drug products.

Though incremental innovations may be cost-effective in specific circumstances, drug benefit policies typically add medicines to their formularies on a discrete, yes/no basis. When a product is approved for reimbursement under a plan or on a formulary, utilization decisions are generally left to participants in the clinical encounter: physicians and patients. Often, neither prescribing physicians nor insured patients have an incentive to consider financial implications of selecting high-cost medicines when lower cost alternatives may fare as well or, in some cases, even better. Physicians and, increasingly, patients receive much of their drug-related information through promotional materials—source ranging from company sponsored continuing medical education events, to television ads for a particular brand of cholesterol drug. The combined influences of these financial incentives and information sources make it possible (indeed, probable) for the excessive utilization of newer, higher price medicines (Berndt et al., 2000; Morgan, 2000, 2001a). Policies can be designed to counteract these effects to some extent; examples of such policies are discussed and simulated below.

1.3.1 Generic Substitution

Generic substitution policies represent an example of utilization management techniques aimed at providing patients (and, to a more limited extent, providers) the financial incentive to consider the relative costs and benefits of competing, therapeutically equivalent products.

Generic drugs are different from "no-name" consumer products such as peanut butter, in that they are all government certified to be chemically equivalent to the original brand name product.

Generic drugs are chemically equivalent competitors of brand name pharmaceuticals, which often enter the market following the expiry of patents held on the brand name product. While generic drugs are often sold under the generic name of their active ingredients, they should not be regarded as merely the pharmaceutical equivalent of generic consumer goods such as "no-name" peanut butter. Unlike "no-name" consumer goods, all generic drugs are government certified to be chemically equivalent to the original brand name product. Before being brought to market, they must meet standards for chemical identity, purity and potency, as well as manufacturing standards and labelling restrictions. In clinical terms, there is no scientific evidence of systematic differences in outcomes across countries, drug plans, or hospitals with widely varying rates of generic drug use (FDA, 2002).

Differences between drugs that are government certified as chemically equivalent are limited to packaging, non-active ingredients and possibly colour or shape. These minor differences may be important to some individuals. Some patients may react to the non-active ingredients in the brand or the generic

version of a particular drug; some patients may greet a change in the colour or shape of their medicine with anxiety; and some patients may be loyal to certain brands or companies for other reasons. In all of these cases, the patient prefers a particular version of a product.

Some indication of the value consumers place on brand name drugs may be inferred from the fact that, in some settings, brand name drugs remain in wide use after lower cost generics become available. Several studies have shown that when generic drugs have entered U.S. markets at substantial discounts relative to their brand name competitors, large numbers of patients (in many cases a majority) have continued to purchase the brands (Caves et al., 1991; Grabowski and Vernon, 1992; Griliches and Cockburn, 1994; Frank and Salkever, 1997). Moreover, in response to entry by generic competition, brand name drug manufacturers often engage in a form of "cream-skimming," whereby they increase their price and serve a market segment of "brand-loyal" customers. That consumers continue to purchase the brand name products in the face of widening price differentials may indicate that those consumers perceive the value of the brand name drug to be much greater than generic alternatives. For other consumers, on the other hand, switching to generic drugs represents a cost-savings. Because generics are chemically equivalent to brand name products, the amount of savings implicit in switching may be significant—provided that the price of generics are significantly lower than brands.

Hospital operating costs are kept down by almost exclusive use of the generic drug, when available.

The use of generic drugs varies considerably across contexts. Within Canadian hospitals, where pharmaceutical costs are a component of overall operating expenses paid for by provincial governments, therapeutics committees set restrictions on drug use, including generic substitution. Consequently, hospitals typically use generic drugs almost exclusively when available. Outside the hospital setting, generic drug use is influenced by legal and administrative factors. Canada's federal and provincial governments have long encouraged generic drug use in the ambulatory setting by accepting liability when certified equivalent generic drugs are substituted for their brand name competitors. Moreover, most Canadian provinces have put in place policies that encourage the use of generic drugs when available. Some provinces, such as Ontario and Saskatchewan, take the approach of actively managing the prices and use of generic drugs for purchases made under publicly administered drug plans. Other provinces take a more laissez faire approach to managing generic utilization. Influenced by these differences, generic use as a percentage of all prescriptions filled in the 12 months ending June 2002 (including those for which there are no generic alternatives) varied from a low of 35% in Quebec to a high of 46% in Saskatchewan, with a national average of 40% (IMS, 2002). Forty-three per cent of prescriptions dispensed in Manitoba during 2002 were for generic drugs.

Generic drug use will result in savings in proportion to the relative price-discount that generics offer vis-à-vis brand name alternatives. Provincial governments have applied limited price setting policies for generic drugs. The Ontario government has been able to use its purchasing power to place across-the-board restrictions on generic drug prices. The Ontario government requires that the first generic entrant into a product market be priced 30% below the brand and that each successive generic entrant must be priced 10% below its generic competitors. Saskatchewan uses its purchasing authority to obtain competitive drug prices in multi-source product classes. It does so by tendering standing offer contracts to the lowest cost supplier. The winners of these auction-style price negotiations are guaranteed virtually all of the provincial market for a fixed period of time.

To encourage generic use and generic discounts, several provinces use a steering charge that applies to the choice of brand versus generic drug products. Known as tier one reference pricing in many jurisdictions around the world, these policies provide reimbursement at a level equal to the cost of the least expensive product among a group of chemically equivalent products. By setting the reimbursement level equal to the lowest cost alternative in a product class, such policies may foster generic discounts by creating competition between generic suppliers. Generic use is fostered by the incentives given to patients. Beneficiaries of plans with such policies are free to pay the difference between the generic product and the preferred brand should they prefer to receive the brand. In cases where a generic drug proves intolerable on clinical grounds, patients generally receive the brand name product at no charge. The impact of these policies has been to reduce public expenditure substantially for multi-source drugs, without limiting access to needed medicines (Grootendorst et al., 1996; Fassbender and Pickard, 2000). Cross-provincial evidence does not, however, suggest that these policies generate greater generic discounts than those attained through standing offer contracts or compulsory discount schemes (PMPRB, 2002).

1.3.2 Reference Pricing and Therapeutic Interchange

In an attempt to manage choices among therapeutically similar but chemically distinct products, prescribing protocols, special authority restrictions, and reference based pricing mechanisms are being used by many drug benefits managers in Canada (Morgan et al., 2003). Prescribing protocols typically require that designated first-line treatment options be tried and exhausted before higher cost therapies are eligible for reimbursement. Special authority policies allow coverage for only those patients who meet clinical criteria known to render higher priced medicines cost-effective. Finally, reference based pricing policies reimburse patients using any of the products within a class of close-substitutes according to the price of the lowest cost product within that class. Reference pricing policies typically involve special authori-

ty exemptions for patients that have clinical reasons for using a particular product within the class. Each of these policies moves the centralized coverage decision from one that is discrete (covered or not), to one that is conditional (covered under certain circumstances, but not in general). In doing this, these policies ensure continued access to therapy while mitigating the financial incentive for patients to engage in moral hazard: i.e., the utilization of higher cost medicines merely because someone else is paying for them.

One way to reduce costs is to encourage the use of older, cost-effective drugs.

When generic drugs are priced competitively, and their use encouraged, savings from generic drug use is dependent on policies that promote off-patent drug prescribing. One approach to encouraging the use of older, cost-effective drugs is therapeutic reference pricing. This incentive pricing strategy encourages the use of cost-effective products among groups of drugs that are closely related but chemically distinct, and/or encourages competing manufacturers to price newer products at levels that are comparable to those of established treatments.

The savings generated from B.C.'s reference drug program is in the tens of millions of dollars.

The British Columbia Pharmacare program implemented therapeutic reference pricing for three categories of drugs in 1995 and two additional categories in 1997. Under these policies, the drug plan reimburses dispensing pharmacies an amount equal to the cost of the reference product within the five classes of therapeutically similar but chemically distinct drugs. Patients can pay the difference between the cost of the product prescribed to them and the "reference" amount the drug plan contributes. As with generic substitution policies, special exemptions ensure that patients with clinical reasons for receiving a specific product are not constrained by the reference pricing policy. British Columbia's reference drug program has been successful at reducing costs within the therapeutic categories to which it has been applied. Moreover, these reductions do not appear to have adversely affected plan beneficiaries' access to medicines or health outcomes. Accumulated over time, the savings generated from British Columbia's reference drug program is measurable in the tens of millions of dollars, while there has been no evidence of systematic deterioration in the quality of therapy received by beneficiaries covered under the program (Braae et al., 1999; Grootendorst et al., 2001; Maclure et al., 2001; Marshall et al., 2002; Schneeweiss et al., 2002; Schneeweiss et al., 2002; Schneeweiss et al., 2002).

1.4 Background: ACEIs and A2RAs

The use of beta-blockers and diuretics has decreased throughout the 1980s and 1990s, while the use of ACEIs and A2RAs has increased (Manolio et al., 1995; Siegel and Lopez, 1997). The incident use of ACEIs in elderly Canadians with newly-diagnosed hypertension increased from 4.1% in 1994 to 4.5% in 1997 (Maclure et al., 1998; McAlister et al., 2001). There is a growing literature which shows that ACEIs reduce mortality after myocar-

dial infarction (Huckell et al., 1997). The first ACEI, captopril, was released in the early 1980s, followed by newer, "me-too" ACEIs and then the angiotensin receptor antagonists (A2RAs) in the mid- to late-1990s. ACEIs and A2RAs have a similar pharmacologic action and both are used to treat congestive heart failure and hypertension. The clinical effects of A2RAs are similar to ACEIs in terms of blood pressure lowering, but A2RAs have a lower prevalence of adverse effects normally associated with ACEIs, such as cough and angioedema. A2RAs are generally more expensive than ACEIs. Therefore, A2RAs are usually reserved for those who cannot tolerate ACEI's side effects.

A recent MCHP study (Metge et al., 2003) examined the appropriateness of use of ACEIs and A2RAs following the 1999 Canadian Hypertension Guidelines, which emphasize the importance of cardiovascular risk assessment and provide recommendations for the treatment of hypertension according to the presence of cardiovascular comorbidity (Feldman et al., 2000). ACEIs are listed as drugs of choice for hypertension coexisting with diabetes, congestive heart failure or renal failure and are alternate drugs of choice for uncomplicated hypertension. Hypertension coexisting with diabetes and congestive heart/renal failure accounted for an increasingly greater share of new ACEI use in 1999/2000 than in 1996/97.

A2RAs were used increasingly more often over the four-year period in persons with and without previous ACEI prescriptions. The former scenario represents switching, potentially due to the cough side effects of ACEI. Switching occurred to a greater extent in persons with coexisting diabetes and congestive heart/renal failure than uncomplicated hypertension, which may be the outcome of new evidence for the renal protective properties of A2RAs in diabetic nephropathy (Garg et al., 2002). A2RA prescription users with no previous prescriptions for ACEIs experienced the steepest growth in use from 0.5% of persons with hypertension in 1996/97 to 1.7% in 1999/2000, accounting for 64% of all new A2RA users in 1999/2000. Treatment for hypertension with a comorbid condition did not account for an increasing share of new A2RA use in the absence of previous ACEI treatment. Further, the per cent of persons with new prescriptions for A2RAs as first-line agents in newly-diagnosed hypertension increased fourfold over this four-year period.

1.4.1 Referencing ACEIs

Owing to evidence that ACEI products of varying vintages—from pioneering ACEI products to recently launched me-too products—exhibited very similar therapeutic effects, but commanded significantly different costs per case treated, the British Columbia government included ACEIs in its reference drug program in January 1997. The government set a fixed, "reference"

price for ACEI products that was based on the average cost per day of treatment with the pioneering product, captopril. Patients could pay the difference between this reference amount and any product within the class that they or their physicians preferred on non-clinical grounds. Generous opportunities were made to exempt patients from therapeutic substitution when there were any clinical grounds for doing so. Exemptions included patients receiving prescriptions from cardiovascular specialists, patients with a history of diabetes or asthma, and any patient for whom a physician filed an exemption form on the grounds of "frailty" or a previously failed trial of the reference drug.

Of B.C. seniors receiving ACEI products before the policy change, 36% were either using the "reference" products or had a history of diabetes, asthma or specialty care (Schneeweiss et al., 2002; Schneeweiss et al., 2002). These individuals were in no way affected by the policy. Furthermore, owing in part to the generous nature of the exemptions, over half (52%) of ACEI users that received high-cost, non-reference products were exempted from the policy on the basis of "frailty." Of those who were not exempted from the policy, patients either paid additional costs out-of-pocket, or "switched" to drugs priced at or below the reference amount. Persistence on therapy was equivalent between those who switched to cheaper drugs and those who stayed on the high-cost medicines. Therefore, out-of-pocket charges born by those who chose to remain on higher cost treatments did not appear to impede treatment access.

Opponents to reference pricing argued that it would have a significant, detrimental affect on those who would "switch" treatments as a result of the reference policy. In British Columbia, "switchers" exhibited a temporary increase in the use of physician services in the months just prior to and following the policy change. This temporary increase in medical service use was, in all likelihood, necessary for changing ongoing (renewable) prescriptions, and related increases inpatient monitoring. There were no long-term increases in health service use by these patients, nor evidence of deleterious health impacts.

2.0 METHODS

2.1 Drug Classes and Patient Cohorts

This analysis focuses on ACEI and A2RA drugs, which are commonly used for the ongoing management of hypertension and/or the treatment of other cardiovascular conditions. We define the ACEI and A2RA drug product classes according to the World Health Organization Anatomical Therapeutic Classification system. The first four digits of ACEI drugs are C09A and C09B; those for A2RA drugs are C09C and C09D. The cohort of patients studied here is therefore patients who filled one or more prescription from these therapeutic categories over the period from 1998/99 to 2000/01.

The patient cohort for this study is defined according to the use of drug products. The goal is to investigate the potential impact of alternative pricing and utilization management strategies within these therapeutic classes.

The patient cohort for this study is defined according to the use of drug products. This differs from analytical approaches that define cohorts based on medical records or other means that identify the clinical condition a priori. An example of the latter approach would be to look for diagnoses in medical service files that indicate hypertension and then to look for exposure to ACEI and A2RA drugs within the cohort of patients with such a diagnosis.

Our focus on all users of ACEI and A2RA drugs reflects the nature of potential policy interventions that we are assessing. Our goal is to investigate the potential impact of alternative pricing and utilization management strategies within these therapeutic classes. We stratify users of ACEI and A2RA drugs according to relevant morbidities in the policy simulations, but operate under the assumption that the pricing and utilization management policies would not be conditional on the primary diagnosis of hypertension. Furthermore, as discussed above, an overarching assumption within this analysis is that prescribing from these classes was appropriate in the first place—i.e., that these patients should have been treated pharmacologically and, in particular, with ACEIs or A2RAs rather than other anti-hypertensive/cardiovascular treatments.

2.2 Patterns of Use and Cost

The initial data analysis of the ACEI and A2RA market dynamics is the tabulation of the basic utilization and cost patterns. This serves as a basis for identifying parameters for the ACEI reference pricing simulation, and gives useful information regarding the relationship between product volume and product prices. We conducted the base trend analysis on quarterly aggregates. This provides useful information with respect to seasonal patterns of use without creating the noise—in particular, the frequent "zero" observations for specific drug products—that often accompanies monthly analysis.

The following measures were constructed to measure the trends and patterns of expenditure and utilization patterns:

Total Public Cost: The total amount the government spent toward the purchase of prescriptions dispensed. These public expenses included Pharmacare expenses after patients had reached their individual deductibles, as well as payments under the Family Services plan and the Non-Insured Benefits plan for First Nations people.

Total Private Cost: The total amount not paid by Manitoba Health toward the purchase of prescriptions dispensed. This is referred to as private sector costs and includes payments through private insurance or out-of-pocket individual expenditures incurred before patients reached their individual deductibles under the Pharmacare plan.[1]

Ingredient Cost: The total amount paid for ingredients in the prescriptions dispensed.

Dispensing Fees: The total fees charged on per prescription basis by pharmacists for prescriptions dispensed.

Access: The number of discrete patients filling one or more prescription for any drug within the product class.

Prescriptions Dispensed: The number of prescriptions filled. Note: this analysis does not account for prescriptions written but not filled.

Units Dispensed: The number of natural units dispensed. These units are typically pills or tablets, and vary in strength.

Defined Daily Doses Dispensed: Because pills and tablets contain different ingredients at different strengths, the World Health Organization's Defined Daily Dose (DDD) measures were used to estimate the number of days of therapy represented by a prescription for a given quantity of a given active ingredient.

Prescribed Days Supplied: The total number of "days supplied" as recorded on the prescription records in the DPIN database. This measure indicates the intended number of days of therapy represented by a given prescription. It can be used to calculate the intended daily dosage for patients receiving treatment, which may differ from the standardized "Defined Daily Dose."

[1] Also included were prescriptions reimbursed by some private plans and prescriptions paid out-of-pocket, as these prescriptions could not be identified separately.

2.2.1 Analysis

Descriptive analyses of trends in use and costs were conducted within and across the aggregate classes of ACEIs and A2RAs, and separately for each "product." A drug "product" was considered an identity unique to the level of active ingredient, dosage form, strength, and supplier type—i.e.; we separate brand name suppliers from generics, but do not distinguish between competing generic suppliers of the identical product. Various strengths of captopril, for example, are supplied in both brand name form ("Capoten," made by Squibb Canada Inc.) and in generic form (captopril, made by Apotex Inc., Novopharm Inc., Genpharm Inc., Pharmascience Inc., Nu-Pharm Inc. and others). We list each strength of the product under the two headings of "brand" and "generic." "Generic" therefore contains sales by often-multiple manufacturers.

2.3 Findings: Overall Costs and Utilization Patterns

Detailed analysis of ACEI and A2RA market dynamics was conducted for the period between 1998/99 and 2000/01. This section contains overall market trends and patterns of access. The following sections investigate intra-class dynamics in detail.

Costs for ACEI and A2RA drug products grew 40% in the two years 1998/99 to 2000/01. This translates into an annual growth rate of 12%, well above the 7% annual growth in national prescription drug expenditures during these years.

Total Costs: As illustrated in Table 1, total spending on ACEI and A2RA drug products grew from $19.7 million in 1998/99 to $27.8 million in 2000/01. This increase of $8.1 million or 40% in two years translates into an annual growth rate of 12%, well above the 7% annual growth in national prescription drug expenditures during these years (CIHI, 2002).

Table 1: Costs, access, and days supplied for ACEI and A2RA drugs, 1998/99-2000/01

	1998/1999	1999/2000	2000/2001	Annual Growth Rate
Total Cost	$19,712,726	$22,739,183	$27,854,142	12%
% Public	39%	39%	40%	
Ingredient Cost	$17,328,999	$19,862,544	$24,225,574	12%
% Public	39%	38%	39%	
% of Total Cost	88%	87%	87%	
Dispensing Fees	$2,383,727	$2,876,640	$3,628,568	15%
% Public	42%	42%	42%	
% of Total Cost	12%	13%	13%	
Access	188,719	217,193	253,745	10%
Total Cost Per	$104.46	$104.70	$109.77	
Ingredient Cost Per	$91.82	$91.45	$95.47	
Prescriptions	372,812	436,795	520,469	12%
# Per Patient	2	2	2.1	
Total Cost Per	$52.88	$52.06	$53.52	
Ingredient Cost Per	$46.48	$45.47	$46.55	
Dispensing Fee Per	$6.39	$6.59	$6.97	
DDDs	18,646,386	22,640,149	27,799,339	14%
# Per Prescription	50	52	53	
Total Cost Per	$1.06	$1.00	$1.00	
Ingredient Cost Per	$0.93	$0.88	$0.87	
Days Supplied	16,671,775	19,381,128	22,691,826	11%
# Per Prescription	45	44	44	
Total Cost Per	$1.18	$1.17	$1.23	
Ingredient Cost Per	$1.04	$1.02	$1.07	

Total Public Cost: The total amount the government spent toward the purchase of prescriptions dispensed in the ACEI and A2RA categories exhibited a predictably cyclical pattern within years, with steady growth between years. In each year of analysis, the government financed approximately 39% of total spending on these products. However, the percentage of spending covered by government was approximately 17% in the first quarter of each year, significantly lower than the approximately 57% of fourth quarter spending that was publicly financed. Although disease patterns have a cyclical nature, this pattern of financing reflects the increased uptake of public benefits as annual deductible levels are reached over the course of the year. Below-deductible spending necessarily takes place before public benefits kick-in. Therefore, public spending accounts for a lower proportion of spending in the first quarters of the year than it does in the latter quarters of the year.

Total Private Cost: The total amount paid through private insurance or out-of-pocket individual expenditures year-over-year growth that was almost identical to the overall growth in public expenditures. Consequently, the private share of yearly expenditures remained constant. The quarterly private share of total spending on ACEI and A2RA drugs exhibited cyclical patterns that mirror the cyclical public shares.

Ingredient Cost: Ingredient costs, the amount paid for the pills and tables dispensed for prescriptions filled, grew at a rate just slightly lower than the growth in total costs for ACEI and A2RA prescriptions dispensed. The ingredient costs accounted for 88% of total spending on ACEI and A2RA drugs in 1998/99, and 87% in 1999/2000 and 2000/01. The public share of ingredient costs was approximately equal to the public share of total expenditures on prescriptions for these products.

Dispensing Fees: The total fees charged on per prescription basis by pharmacists for ACEI and A2RA prescriptions dispensed increased at a faster rate than ingredient costs. They accounted for 12% of total costs in 1998/99, and 13% in 1999/2000 and 2000/01.

Access: The number of patients filling one or more prescription for any drug within either the ACEI or A2RA product classes during any given quarter increased from almost 43,882 individuals to 67,501. This represented a 54% increase in the rate at which the population accesses these products. The total cost per patient receiving one or more prescriptions from these classes increased by 20% over the period of analysis, from roughly $98 to $118.

Prescriptions Dispensed: The number of prescriptions filled for either ACEIs or A2RAs increased more quickly than the number of patients receiving them. The quarterly volume of prescriptions received by patients

increased from approximately 83 thousand to 143 thousand, or 73%, over the period. This growth in quarterly dispensation is slightly greater than the 40% increase in annual dispensation due to the seasonal differences in drug use and because prescribing rates grew steadily both across and within years. Because growth in prescriptions outpaced the number of patient recipients, the average number of prescriptions received per patient in a given quarter increased by 12%, from 1.89 to 2.13. The total cost per prescription dispensed increased by 7% over the period.

Defined Daily Doses Dispensed: Because pills and tablets contain different ingredients at different strengths, the World Health Organization's Defined Daily Dose (DDD) measures were used as on method of estimating the number of days of therapy represented by a prescription for a given quantity of a given active ingredient. The DDD measure is included in the descriptive statistics because it is a commonly used in population-level drug utilization research. The number of defined daily doses dispensed to patients receiving either ACEIs or A2RAs increased by 96% over the period. This increase may, however, overstate true therapeutic volume due to changes in the dosages received per patient over time. Defined daily doses are based on estimates of the average dose used according to the primary indication for a drug. Actual therapeutic use of a drug may vary considerably; this variation reduces the validity of DDDs. For example, if a large male patient receives a higher dosage of than a smaller female patient does, DDDs count the consumption of the male patient is counted as "more" consumption than that of the female. This may not generally be desirable.

Prescribed Days Supplied: The total number of days of therapy represented by prescriptions dispensed for all patients receiving either ACEIs or A2RAs increased by 74% over the period of analysis. This measure trended closely with the number of prescriptions dispensed. The average number of days supplied per prescription was 44 over the three years. Average days supplied per prescription was approximately one day greater in the last quarter of each year than in the first quarter. The average cost per "day supplied" of ACEIs and A2RAs drug products increased by 6% over the period of analysis.

2.4 Findings: Cost and Utilization Patterns by Product Class

Costs: Table 2 lists the use and cost trends by source of payment. Annual expenditures on ACEI products (dispensing fees and ingredient costs included) grew by 27% over the period. This 8% annual growth rate is roughly equal to the 7% national growth in prescription drug costs over the period (CIHI, 2002). Expenditures on A2RA drugs, on the other hand, grew at a rate far exceeding average national prescription drug expenditure rates.

In Manitoba between 1998/99 and 2000/01, annual expenditures on A2RA products grew by 136%, a 33% annual rate of growth.

Annual expenditures on A2RA products in Manitoba grew by 136% over the period, a 33% annual rate of growth. Because the growth in expenditures on A2RA drugs far exceeded the growth in expenditures on ACEI products, the share of the combined market spending spent on the A2RA product class increased from 11% to 23% between 1998 Q2 to 2001 Q1.

Table 2: Costs, access, and days supplied by category and payment source, 1998/99-2000/01

	1998/1999	1999/2000	2000/2001	Annual Growth Rate
ACEI	$17,154,168	$18,331,655	$21,805,090	8%
% Public	39%	40%	41%	
% of Total Market	87%	81%	78%	
A2RA	$2,558,558	$4,407,529	$6,049,052	33%
% Public	38%	34%	35%	
% of Total Market	13%	19%	22%	
Ingredient Cost				
ACEI	$15,058,949	$15,954,050	$18,895,312	8%
% of Total Cost	87%	80%	78%	
A2RA	$2,270,050	$3,908,494	$5,330,262	33%
% of Total Cost	13%	20%	22%	
Access				
ACEI	168,033	181,753	205,611	7%
Ingredient Cost Per	$89.62	$87.78	$91.90	
A2RA	22,757	38,565	52,630	32%
Ingredient Cost Per	$99.75	$101.35	$101.28	
Days Supplied				
ACEI	14,786,242	16,104,797	18,178,554	7%
Ingredient Cost Per	$1.02	$0.99	$1.04	
A2RA	1,885,533	3,276,331	4,513,272	34%
Ingredient Cost Per	$1.20	$1.19	$1.18	

A2RA drugs increased at an annual rate of 32%, whereas the rate for ACEI drugs increased by 7%, over the same period.

Access: Changes in the pattern of access across the ACEI and A2RA product categories mirrored the changes in expenditures. The rate at which Manitoban's accessed ACEI drugs increased at an annual rate of 7% over the period, whereas access to A2RA drugs increased at an annual rate of 32%.

The cost per patient accessing ACEI drug products declined during 1999/2000, and then returned to a 2000/01 level that was 2% higher than the 1998/99 level. The cost per patient accessing treatments within the A2RA category grew slowly, but consistently through to 2001/02, increasing by 2% over the three years.

The average costs per patient accessing A2RA drugs in Manitoba was 10% higher than the average cost per patient accessing ACEI drugs in 1998/99 and 2000/01. Owing to the temporary decline in the cost of ACEI therapy in 1999/2000, the average cost of A2RA therapy was 15% higher than ACEI therapy in that year.

Days Supplied: The patterns of days supplied across the ACEI and A2RA product categories were similar to the patterns of access across these categories. The annual total days of ACEI supplied increased by 23% from 1998/99 to 2000/01. The annual total days of A2RA therapy supplied increased by 139%. The average patient filling one or more A2RA prescription received slightly more days supplied per quarter in 2000/01 than in 1998/99.

2.5 Findings: Cost and Utilization Patterns Within Product Class

Market analysis of dynamics within the ACEI class reveals little evidence of price competition between brand and generic non-patented products or between patented and non-patented drugs.

There are over 16 different types of products (grouped by active ingredients) that could be prescribed to patients from the A2RA and ACEI drug categories—six types of A2RA drug and 10 ACEI drug types. The analysis of market dynamics within the ACEI class (as will be described below) reveals little evidence of price competition between brand and generic non-patented products or price competition between patented and non-patented drugs. One would expect significant price competition between brand and generic drugs, as they are essentially identical products. Furthermore, one would also expect some price competition between different patented and non-patented products within the ACEI product class because clinical data reveal relatively few significant differences between them.

2.5.1 ACEI Market Dynamics

Table 3 contains use and cost information pertaining to the ACEI category, within which market dynamics have been steadily changing. Products based on the pioneering active ingredient in the ACEI category, captopril, account for a small and steadily diminishing share of the total market. Newer products have taken over this market.

Captopril-based products (ACEIs) were one of only two product types to show absolute declines in use. The other product type to show declines was benazepril, which was used by fewer than 400 Manitobans, at any point in the period of analysis.

Captopril was brought to the market in the early 1980s in various strengths and forms. Generic versions of captopril products began to come onto the Canadian market shortly thereafter, owing to compulsory licensing provision of Canadian patents for pharmaceuticals. By 1998/99, the beginning of this analysis, captopril-based products accounted for only 6% of sales, 7% of patients' accessing ACEI treatment, and 7% of total ACEI days supplied. By 2000/01, each of these measures of captopril market share had fallen to only 3%. Captopril-based products were one of only two product types to show absolute declines in use (and consequently expenditures). The other product type to show declines in absolute use was benazepril, an ACEI used by fewer than 400 Manitoban's at any point in the period of analysis.

Table 3: Costs, access, and days supplied within ACEI category, 1998/99-2000/01

	1998/1999		1999/2000		2000/2001		Annual Growth Rate
Total Cost							
Captopril	$974,212	6%	$805,880	4%	$638,416	3%	-13%
Enalapril	$7,570,744	44%	$7,040,755	38%	$7,622,640	35%	0%
Lisinopril	$2,907,457	17%	$3,131,763	17%	$3,358,940	15%	5%
Perindopril	$234,802	1%	$324,909	2%	$439,798	2%	23%
Ramipril	$670,142	4%	$1,087,826	6%	$2,636,062	12%	58%
Quinapril	$1,050,947	6%	$1,153,859	6%	$1,312,910	6%	8%
Benazepril	$122,455	1%	$108,417	1%	$97,508	0%	-7%
Cilazapril	$837,567	5%	$1,048,990	6%	$1,163,283	5%	12%
Fosinopril	$2,108,159	12%	$2,680,289	15%	$3,186,919	15%	15%
ACEI + Diuretic	$677,684	4%	$948,966	5%	$1,348,616	6%	26%
Access							
Captopril	11,233	7%	8,953	5%	6,928	3%	-15%
Enalapril	62,812	37%	61,166	33%	58,264	28%	-2%
Lisinopril	32,098	19%	33,659	18%	34,899	17%	3%
Perindopril	2,863	2%	3,815	2%	4,869	2%	19%
Ramipril	7,570	4%	12,214	7%	28,276	14%	55%
Quinapril	10,967	6%	11,945	7%	13,522	7%	7%
Benazepril	1,484	1%	1,259	1%	1,081	1%	-10%
Cilazapril	9,922	6%	12,115	7%	13,057	6%	10%
Fosinopril	23,122	14%	28,200	15%	32,341	16%	12%
ACEI + Diuretic	7,058	4%	9,818	5%	13,734	7%	25%
Days Supplied							
Captopril	961,286	7%	772,374	5%	603,605	3%	-14%
Enalapril	5,534,227	37%	5,421,270	34%	5,149,364	28%	-2%
Lisinopril	2,864,637	19%	3,015,045	19%	3,124,647	17%	3%
Perindopril	229,072	2%	312,429	2%	406,938	2%	21%
Ramipril	646,003	4%	1,029,219	6%	2,402,650	13%	55%
Quinapril	964,453	7%	1,056,703	7%	1,194,887	7%	7%
Benazepril	131,938	1%	114,190	1%	98,486	1%	-9%
Cilazapril	844,982	6%	1,050,811	7%	1,131,755	6%	10%
Fosinopril	2,011,028	14%	2,502,106	16%	2,890,096	16%	13%
ACEI + Diuretic	598,616	4%	830,650	5%	1,176,126	6%	25%

The market leader in the ACEI class was enalapril.

The market leader in the ACEI class was enalapril. Enalapril-based products had been the market leaders in 1998/99, with 44% of sales volume and 37% of patients and days supplied. Enalapril expenditures declined precipitously in 1999/2000, without a commensurate decrease in the number of patients receiving enalapril-based products or the number of days of enalapril therapy supplied. While utilization did fall, the cost per patient treated or day of treatment declined significantly for enalapril-based products in 1999/2000. The consequence of theses dynamics for the enalapril-based products competing within a larger and growing market segment (ACEIs) was that the enalapril share of total ACEI sales and use declined over the period of analysis.

Ramipril sales increased dramatically—nearly four-fold—in Manitoba from the fall of 1999 to early 2001. This was largely due to a rapid increase in the number of patients being prescribed ramipril.

The major gain in ACEI market share was made by products based on ramipril. The rate of prescribing ramipril was dramatically increased in the fall of 1999, when a large (and largely Canadian) clinical trial showed it was effective in the secondary prevention of cardiovascular disease among certain populations (Tu et al., 2003). The results of the Heart Outcomes Prevention Evaluation (HOPE) trial were presented at a conference in Europe in August 1999, received newspaper publicity in September 1999, and were published in the New England Journal of Medicine in January 2000. Ramipril sales increased nearly four fold in Manitoba from the fall of 1999 to early 2001, this was largely due to a rapid increase in the number of patients receiving ramipril prescriptions.

This increase in prescriptions ". . . was due more to hype than to HOPE, as the striking increase was out of proportion to the evidence supporting use of this drug and was mostly in response to intense marketing" (Pilote, 2003).

It is noteworthy that the effects of ACEI products are generally considered class-effects, and that the published findings concerning ramipril likely generalize to all ACEIs (Pilote, 2003; Tu et al., 2003). However, intensive marketing and public relations drove the market response; as one reviewer put it, " . . . the rise in ramipril prescribing was due more to hype than to HOPE, as the striking increase was out of proportion to the evidence supporting use of this drug and was mostly in response to intense marketing" (Pilote, 2003).

2.5.2 Cost of Therapy and Within ACEI Category

The cost per day supplied of ACEI products is illustrated in Table 4. The competitive dynamics within the market for ACEI products indicate that the demand for a product is not related to its cost. This is illustrated by the levels of and changes in average costs per day of therapy of the different types of ACEI drugs over the period of analysis. The market dynamics for the leading product types, in particular, are counter to that which would be predicted by conventional, competitive market theory.

The competitive dynamics within the market for ACEI products indicate that the demand for a product is not related to its cost.

Table 4: Cost per day supplied within ACEI category, 1998/99-2000/01

	1998/1999	1999/2000	2000/2001	Annual Growth Rate
Cost Per Day Supplied				
Captopril	$1.01	$1.04	$1.06	1%
Enalapril	$1.37	$1.30	$1.48	3%
Lisinopril	$1.01	$1.04	$1.07	2%
Perindopril	$1.03	$1.04	$1.08	2%
Ramipril	$1.04	$1.06	$1.10	2%
Quinapril	$1.09	$1.09	$1.10	0%
Benazepril	$0.93	$0.95	$0.99	2%
Cilazapril	$0.99	$1.00	$1.03	1%
Fosinopril	$1.05	$1.07	$1.10	2%
ACEI + Diuretic	$1.13	$1.14	$1.15	0%

Within the ACEI category of products, the average cost per day of therapy supplied in Manitoba varied by almost 50% in 1998/99. The highest cost product per day of treatment supplied was, ironically, one of the only products subject to generic competition at the time: enalapril. The average cost of a day's supply of enalapril was $1.37 in 1998/99, whereas the cost per day's supply of virtually all other leading ACEI products was approximately $1.00 at the time. As mentioned previously, enalapril based products were used by 37% of the population receiving ACEI drugs in the period, which represented 44% of total market revenues due to their relatively high-cost per day of treatment.

The difference between highest and lowest cost ACEI products declined slightly in 1999/2000, when the prices of generic versions of enalapril were substantially discounted (more below). This change in the average cost of enalapril-based therapy occurred at the same time as a decline in the share of ACEI patients receiving enalapril-based products. That is, demand for these specific products declined while competition was reducing their prices. As the average cost per day of enalapril-based therapy increased in 2000/01, the decline in demand continued. Mirroring the trend in demand for enalapril was the increase in the use of ramipril in 1999/2000 and 2000/01. This increase in demand occurred at a time when the average cost of a day's supply of ramipril increased by 4%.

2.5.3 A2RA Market Dynamics

The dynamics within the A2RA market segment—illustrated in Table 5—are characteristic of new product classes. The pioneering product, losartan, captured almost two-thirds of the market (63%) in 1998/99. While maintaining a modest 2% rate of sales growth over the period, the dominant position of losartan was rapidly eroded by the explosive sales of new, competing products. Sales of products based on irbesartan, in particular, rose from 7% of the overall A2RA market to 25%.

Table 6 illustrates the cost per day of treatment within the A2RA market segment did not vary substantially between products or over time.

As Table 6 illustrates, the cost per day of treatment within the A2RA market segment did not vary substantially between products or over time. A day's supply of A2RA therapy was priced at or near $1.33 for all products, including late entrants. This average cost per day of treatment was significantly higher than the average cost per day's supply of ACEI drugs, most of which were priced at approximately $1.00 per day of treatment.

The premium price of A2RA therapies, regardless of their vintage relative to other A2RAs, is indicative of a market segment that competes on the basis of product differentiation. It is notable that the leading ACEI drug, enalapril, and leading A2RA drug, losartan, are both made by Merck Frosst Canada. A firm in such a position may chose to maintain a premium price

on its ACEI drug, even at the expense of ACEI sales, in order to establish a relatively high benchmark for pricing its A2RA.

Table 5: Costs, access, and days supplied with A2RA category, 1998/99-2000/01

	1998/1999		1999/2000		2000/2001		Annual Growth Rate
Total Cost							
Losartan	$1,605,250	63%	$1,729,790	39%	$1,695,349	28%	2%
Valsartan	$293,296	11%	$708,373	16%	$943,844	16%	48%
Irbesartan	$173,230	7%	$1,092,153	25%	$1,487,026	25%	105%
Candesartan	$0	0%	$214,787	5%	$599,263	10%	
Telmisartan	$0	0%	$17,533	0%	$287,391	5%	
A2RA + Diurectic	$486,782	19%	$644,892	15%	$1,036,178	17%	29%
Access							
Losartan	13,994	61%	14,897	38%	14,486	27%	1%
Valsartan	2,821	12%	6,363	16%	8,279	16%	43%
Irbesartan	1,805	8%	9,788	25%	13,027	25%	93%
Candesartan	0	0%	2,041	5%	5,245	10%	
Telmisartan	0	0%	211	1%	2,745	5%	
A2RA + Diurectic	4,261	19%	5,492	14%	9,053	17%	29%
Days Supplied							
Losartan	1,193,842	63%	1,294,504	40%	1,270,899	28%	2%
Valsartan	215,101	11%	529,097	16%	704,229	16%	48%
Irbesartan	124,525	7%	815,330	25%	1,124,384	25%	108%
Candesartan	0	0%	159,362	5%	441,378	10%	
Telmisartan	0	0%	13,482	0%	215,929	5%	
A2RA + Diurectic	352,065	19%	464,556	14%	756,453	17%	29%

Table 6: Cost per day supplied within A2RA category, 1998/99-2000/01

	1998/1999	1999/2000	2000/2001	Annual Growth Rate
Cost Per Day Supplied				
Losartan	$1.34	$1.34	$1.33	0%
Valsartan	$1.36	$1.34	$1.34	-1%
Irbesartan	$1.39	$1.34	$1.32	-2%
Candesartan		$1.35	$1.36	
Telmisartan		$1.30	$1.33	
A2RA + Diurectic	$1.38	$1.39	$1.37	0%

2.6 Generic Competition

Brand name products do not generally discount prices in response to the entry of their generic counterparts. Rather, generics compete for the "price sensitive" market segment by offering substantial discounts.

An important market dynamic in the pharmaceutical sector is competition between branded and generic drugs. Relative price and market share data for generic competitors within the ACEI category are listed in Table 7. It has long been established that brand name products do not generally discount prices in response to generic entry (Grabowski and Vernon, 1992; Griliches and Cockburn, 1994; Berndt et al., 2002). Rather, generics typically compete for the "price sensitive" market segment by offering substantial discounts relative to brand name counterparts.

In Manitoba, various dosage forms of captopril, enalapril, and lisinopril were subject to generic competition at some point over the period of 1998/99 to 2000/01. The price of few of the generics in these market segments seldom fell below 80% of the price of their brand name competitors. Generic versions of captopril and lisinopril offered virtually no discount over corresponding brands, despite moderate (and, in the case of lisinopril drugs, even growing) sales volumes in the categories. Generic manufacturers of captopril products captured over 97% of the market share for each dosage form of captopril. Lisinopril markets, on the other hand, were split along dosage forms. Generics dominated the market for low-dosage lisinopril, with over 87% of market share for 5mg tablets. The brand name manufacturer retained virtually all of the market for higher dosage forms of lisinopril.

Court decisions concerning patents on enalapril dramatically altered generic competition within the ACEI category.

It is notable that generic competition within the ACEI category was dramatically altered by court decisions concerning the patents on enalapril. Patents held by Merck Frosst on enalapril and its salt enalapril maleate had been granted at a time when compulsory licenses could be granted to competing firms under the compulsory licensing provision of the Canadian Patent Act (Eden, 1989; Lexchin, 1993). By 1993, this provision of the Patent Act was abolished. However, compulsory licenses had been granted for the import of enalapril in 1992. Generic manufacturers, notable Apotex and Nu-Pharm, purchased enalapril from a license holder, and sold finished products on the Canadian marketplace. After years of litigation, the courts decided in favour of Merck's claim that any licence pertaining to enalapril was effectively expired by statute on February 14, 1993, and that sale by generic manufacturers was an infringement of patent. The generic supply of enalapril was effectively cut off in the fall of 1999; in 2000 stock that may have been in retail appears to been exhausted quickly. This cycle can be seen in Table 7, where generic versions of enalapril rose from 0% to as high 44% in 1999 and fell back to 1% in 2000/01 as new inventory supply was shut off by the patent ruling.

Table 7: Generic prices and market penetration, ACEI products, 1998/99-2000/01

	1998/1999	1999/2000	2000/2001	Change
Generic Prices Relative to Brand				
Product				
Captopril Tab 12.5mg	100%	100%	97%	-2%
Captopril Tab 25mg	99%	99%	98%	-1%
Captopril Tab 50mg	100%	89%	86%	-14%
Enalapril Maleate Tab 10mg	81%	68%	66%	-15%
Enalapril Maleate Tab 20mg	80%	71%	81%	0%
Enalapril Maleate Tab 5mg	81%	71%	77%	-3%
Enalapril Maleate Tab 2.5mg	80%	71%	81%	0%
Lisinopril Tab 10mg	99%	101%	100%	1%
Lisinopril Tab 20mg	101%	100%	100%	0%
Lisinopril Tab 5mg	98%	100%	86%	-12%
Total Market Value (Brand + Generic)				
Product				
Captopril Tab 12.5mg	$27,131	$21,535	$16,723	-$10,408
Captopril Tab 25mg	$95,111	$73,627	$56,983	-$38,127
Captopril Tab 50mg	$78,448	$70,511	$56,234	-$22,214
Enalapril Maleate Tab 10mg	$615,494	$579,416	$649,851	$34,358
Enalapril Maleate Tab 20mg	$244,902	$254,057	$328,879	$83,977
Enalapril Maleate Tab 5mg	$644,875	$553,382	$556,294	-$88,581
Enalapril Maleate Tab 2.5mg	$195,244	$167,649	$156,213	-$39,030
Lisinopril Tab 10mg	$323,666	$335,356	$343,099	$19,433
Lisinopril Tab 20mg	$194,085	$233,674	$277,963	$83,878
Lisinopril Tab 5mg	$108,002	$105,440	$97,263	-$10,739
Generic Share of Market				
Product				
Captopril Tab 12.5mg	99%	100%	100%	0%
Captopril Tab 25mg	97%	98%	98%	1%
Captopril Tab 50mg	99%	99%	98%	0%
Enalapril Maleate Tab 10mg	0%	43%	1%	1%
Enalapril Maleate Tab 20mg	0%	42%	1%	1%
Enalapril Maleate Tab 5mg	0%	44%	1%	1%
Enalapril Maleate Tab 2.5mg	0%	42%	1%	1%
Lisinopril Tab 10mg	1%	0%	0%	0%
Lisinopril Tab 20mg	0%	0%	0%	0%
Lisinopril Tab 5mg	87%	88%	87%	-1%

2.7 Relative Prices Within and Across Provinces

Provincial reimbursement rates for multi-source ACEI drugs were compared in order to gauge the relative price of generic and brand drugs, in Manitoba.

The estimation of brand name prices includes charges levied to patients. Under the Prescription Costs Act, the government reimburses pharmacists for the lowest priced generic listed as interchangeable. In order to gauge the relative price of generic and brand drugs in Manitoba, we compared reported provincial reimbursement rates for multi-source ACEI drugs. All figures were gathered from publications of the provincial drug plans.

The first comparison was made of the price of generic ACEI drugs relative to their brand name counterparts. Listed in Table 8, this comparison is a within-province comparison, which indicates the relative discount received by the provincial plans for generic drugs dispensed.

Table 8: Generic prices relative to brand (interprovincial comparison), 2003

	Manitoba	British Columbia	Alberta	Saskatchewan	Ontario	Quebec	New Brunswick	Newfoundland/ Labrador	Yukon Territory
Generic									
Captopril - 12.5 mg	1.03	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Captopril - 25 mg	1.03	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Captopril - 50 mg	1.03	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Captopril - 100 mg	1.02	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.02
Lisinopril - 5 mg	0.90	0.80	0.90	0.90	0.75	0.90	1.00	0.88	0.00
Lisinopril - 10 mg	0.94	0.83	0.94	0.94	0.70	0.94	1.00	0.91	0.00
Lisinopril - 20 mg	0.94	0.84	0.94	0.94	0.70	0.94	1.00	0.91	0.00

The Canadian price of generic captopril far exceeds the U.S. price.

The prices for generic captopril products are almost identical to the price of branded captopril in all provinces. This owes in part to a price cut made in 1996 by the manufacture of brand name captopril. Notwithstanding the brand price cut, such harmony of generic prices with the brand is indicative of a lack of competitive forces in the off-patent marketplace. Evidence that the Canadian price of generic captopril far exceeds the U.S. price of generic captopril suggests that the generic price of captopril could be lower in Canada (Graham, 2000).

Reported prices for generic lisinopril products are lower than that of their brand name counterparts in many provinces across Canada. The reported discounts for two of the lisinopril products in Ontario match the 30% required by the Ontario Drug Benefit Program. It is unknown why the generic 5mg form achieves only a 25% discount. British Columbia achieves roughly 15% discount on the lisinopril products. Discounts in other provinces, Manitoba included, are modest at best.

Prices in Manitoba were seven to 9% higher than the provincial average, in eight of the 12 comparisons made. Prices were lower by 3% in only three comparisons.

Each provinces' reported prices relative to the national average of reported prices gives an indication of the interprovincial discounts achieved in some jurisdictions. As can be seen in Table 9, on eight of the 12 comparisons made, prices in Manitoba were 7-9% higher than the provincial average. In only three comparisons were Manitoba prices lower (3%). The reported prices for brand name products in both Quebec and Ontario are consistently lower than national average. The price advantage in these provinces is on a magnitude of three percentage points for most brand name products; however, for generic lisinopril products in particular, Ontario reports a significant (17 to 25%) discount vis-à-vis other provinces.

Table 9: Prices relative to national average (interprovincial comparison), 2003

	Manitoba	British Columbia	Alberta	Saskatchewan	Ontario	Quebec	New Brunswick	Newfoundland/ Labrador	Yukon Territory
Captopril									
Brand - 12.5 mg	1.07	0.97	0.97	1.05	0.97	0.97	0.97	1.06	0.97
Generic - 12.5 mg	1.09	0.97	0.97	1.05	0.97	0.97	0.97	1.06	0.97
Brand - 25 mg	1.07	0.97	0.97	1.05	0.97	0.97	0.97	1.06	0.97
Generic - 25 mg	1.09	0.97	0.97	1.05	0.97	0.97	0.97	1.06	0.97
Brand - 50 mg	1.07	0.97	0.97	1.05	0.97	0.97	0.97	1.06	0.97
Generic - 50 mg	1.09	0.97	0.97	1.05	0.97	0.97	0.97	1.06	0.97
Brand - 100 mg	1.07	0.97	0.97	1.05	0.97	0.97	0.97	1.06	0.97
Generic - 100 mg	1.08	0.97	0.97	1.05	0.97	0.97	0.97	1.06	0.98
Lisinopril									
Brand - 5 mg	0.97	1.10	0.97	1.06	0.97	0.97	0.88	1.09	0.98
Generic - 5 mg	1.00	1.00	1.00	1.08	0.83	1.00	1.00	1.09	
Brand - 10 mg	0.97	1.10	0.97	1.05	0.97	0.97	0.91	1.09	0.97
Generic - 10 mg	1.01	1.01	1.01	1.10	0.75	1.01	1.01	1.10	
Brand - 20 mg	0.97	1.08	0.97	1.05	0.97	0.97	0.91	1.09	0.97
Generic - 20 mg	1.01	1.01	1.01	1.10	0.75	1.01	1.01	1.10	

2.8 Policy Scenarios

In an attempt to illustrate the potential to achieve competitive pricing, four stages of policy have been simulated for the ACEI and A2RA drug classes.

Having thoroughly described the status quo history of these drugs in Manitoba in the recent past, we now investigate the potential impact of hypothetical policy scenarios. To illustrate the potential to achieve competitive pricing among patented and non-patented drug products, together with cost-conscious product selection by patients/prescribers, we simulate four stages of policy for the ACEI and A2RA drug classes. Each of these policy simulations builds in logical sequence, with the cost savings from one policy being largely contingent upon the previous policy being in place. The policies are the following: (1) a policy to promote competitive pricing by generic manufacturers of non-patented ACEI drugs, (2) a policy to promote the selection of available generics by patients, (3) a policy to establish competitive pricing between patented and non-patented ACEI drugs, and (4) a policy to encourage first-line use of ACEI products (step-up care).

Generic Pricing Policy: The market dynamics described above, along with the inter-provincial comparison of list prices for brand and generic drugs, indicate that savings could be gained by achieving lower prices of generic drugs vis-à-vis brand name competitors. The generic pricing policy scenario depicted here is based on the Ontario model. The Ontario government requires that generic entrants in off-patent product markets offer a price that is at least 30% below the brand name product. The generic pricing policy simulation is therefore based on the lower of the following: (1) the actual

price being charged for generic version of a particular ACEI drug in Manitoba, or (2) a price 30% below the actual price being charged for a particular brand name ACEI in Ontario. The generic pricing scenario on its own does not assume that utilization patterns would be altered in any way by the potential reduction in generic prices.

The Generic Substitution Policy depicted here is based loosely on the model used in B.C., Alberta and Ontario.

Generic Substitution Policy: As with generic pricing, the analysis of market dynamics described earlier indicates that greater savings could be achieved through greater use of generic drugs, when available. The generic substitution policy depicted here is based loosely on the model used in British Columbia, Alberta, and Ontario. This policy scenario is one under which the maximum allowable price for multi-source drug products would be the price of the lowest cost alternative, typically the generic drug. Under this policy, patients would be free to pay out-of-pocket for the difference in prices necessary to obtain a higher cost preferred brand, but this amount would not be covered by the government post-deductible and would not count toward patients' deductibles. The impact of this policy is simulated both in conjunction with and independent of the generic pricing scenario described above.

Where similar policies have applied under benefits plans with first-dollar coverage, patients have almost unanimously responded by selecting generic alternatives to brand name drugs. Since drug benefits in Manitoba often involve high deductibles, the impact of the policy may not be as strong for the provincial drug program. However, using the experience of Saskatchewan as a comparator, it is possible that the generic pricing and generic substitution policies can be combined into a tendering process that provides guaranteed sales volume on a compulsory product substitution basis in exchange for further discount from generic suppliers.

No exemptions based on co-morbidity are made in this analysis. Though some patients will find specific drug products (either brand or generics) intolerable due to non-active ingredients, there is no a priori basis for predicting idiosyncratic intolerance. Levels of special exemption on such clinical grounds in other jurisdictions are fewer than 5% of patient populations (Grootendorst et al., 1996).

The Therapeutic Interchange Policy is based on B.C.'s experience with reference based pricing for ACEI drugs.

Therapeutic Interchange Policy for ACEI Drugs: A policy scenario is modelled wherein a maximum allowable cost is established across competing brand and generic drugs in the ACEI product classes. Similar in spirit and based on British Columbia's experience with reference based pricing for ACEI drugs, this policy would set a maximum allowable cost for ACEI drugs based on standard set by the costs of treatment that actually prevail within the product classes or those what would prevail under a scenario where generic pricing was also competitive. The impact of the policy on uti-

lization is not certain, given the fact that suppliers may respond to such a policy by reducing the prices charged for their products, or by encouraging patients to pay the additional cost of their preferred brand.

Special exemptions from this policy scenario are applied for patients with specific co-morbidities and/or those receiving the prescription from a specialist. A patient would be considered exempt from the pricing policy if they have medical histories indicating that they have diabetes (with or without nephropathy), asthma, or had a cardiologist or pulmonary specialist visit in the year of analysis. Those not falling into any of those categories are considered non-exempt. This simulation conforms to the policy experience in British Columbia.

The 'step-up' policy applies only to choices within the ACEI vs A2RA drug products, to encourage first-line use of ACEI drugs.

First-line Use of ACEI Products: The simulated policy to encourage first-line use of ACEI drugs applies only to choices within the ACEI versus A2RA drug products. It is assumed that prescribing one of these types of drugs is appropriate. Conditional on this, the step-up model of care requires that eligible patients be given an ACEI drug trial prior to being prescribed A2RA drugs.

2.9 Morbidity

In 2000/01, approximately 21% of ACEI users were rendered exempt under the morbidity exemption.

Morbidity exemption: A person is considered Exempt if they have been defined, based on our definitions, as having diabetes (with or without nephropathy), or asthma, or had a cardiologist or pulmonary specialist visit. These were the exclusion criteria used in the British Columbia Reference Drug Program, developed by a panel of experts and based on Canadian hypertension guidelines. Those not falling into any of those categories are considered Non-Exempt. For each year, the number of patients qualifying for morbidity exemptions under therapeutic interchange policy scenario is listed in Table 10. Approximately 19% of ACEI users in 1998/99 had coexisting morbidities that would have rendered them exempt under the policy scenario. For these patients, utilization patterns are held constant in the simulation below. In 1999/2000 and 2000/01, approximately 21% of ACEI users had morbidities rendering them exempt from the simulate policy change.

Table 10: Patients qualifying for morbidity exemptions under therapeutic interchange policy scenario, 1998/99-2000/01

	1998/1999	1999/2000	2000/2001
Exempt	35,000	41,000	47,000
Non-Exempt	148,000	158,000	180,000
% Exempt	19%	21%	21%

2.10 Findings: ACEI Policy Scenarios

Simulated here are three generic drug policies and two reference based drug policies that relate to market dynamics within the ACEI category of drugs.

There are a total of five policy simulations that relate to market dynamics within the ACEI category of drugs. Three pertain to the price of generic drugs and policies to encourage their use modelled after the policies in place in Ontario. These three generic drug policies are (1) a policy to encourage (or mandate) generic drug use among multi-source ACEI drug products, (2) a policy to encourage (or mandate) price discounts from generic manufactures, and (3) a policy to encourage both generic price discounts and generic drug use among multi-source ACEIs. We also model two policy scenarios representing attempts to establish therapeutic interchange or competitive pricing between patented and non-patented ACEI drugs. These policies, modelled after the reference drug program in British Columbia, are (4) the approximate savings from reference pricing at prevailing generic prices, and (5) the approximate savings from reference pricing when generic price discounts and generic drug use is also encouraged.

Public savings under the generic discount policy were $78,000 in 2000/01. These modest savings were the outcome of generic drugs not being currently used with significant frequency in Manitoba's ambulatory setting.

We list the level of expenditures and savings accruing to public and private payers for each of the policy scenarios in Table 11. The actual expenditures of the Manitoba government for ACEI drugs were approximately $5.9 million in 1998/99, $6.2 million in 1999/2000 and $7.6 million in 2000/01. Private expenditures for these products were $9.1 million, $9.7 million, and $11.2 million, respectively. Under Option 1 in Table 11, the estimated costs and savings depict a policy scenario wherein generic price discounts are mandated, but generic utilization remains at the actual rate at which generics were selected in the period of analysis. The public savings generated by such a policy start at approximately $139,000 in 1998/99, and decline to $78,000 in 2000/01. Private savings also decline from approximately $203,000 in 1998/99, and $111,000 in 2000/01. The reason for the relatively modest savings from mandating significant discounts from generic suppliers is that generics drugs are not currently used with significant frequency in Manitoba's ambulatory setting. The reduction in potential savings from this policy in 1999/2000 and 2000/01 is a result of the removal of generic versions of enalapril products from the market.

Financial incentives can be made to encourage generic drug use by providing payment at levels equal to generic prices.

In order to collect savings from a policy of mandated generic discounts, generic substitution must be encouraged. While low prices may induce use in conventional marketplaces, this is not generally the case in the pharmaceutical sector. One reason for this is the non-standard financial incentives of prescribers and patients. Policies can encourage generic drug use by providing payment at levels equal to generic prices, thereby providing patients a financial incentive to consider generic alternatives. Several provinces, including Ontario, Alberta, and British Columbia, encourage generic use by requiring patients to pay additional charges if they desire a brand name product.

Table 11: Approximate costs under policies applied to ACEIs only, 1998/99-2000/01

		1998/1999		1999/2000		2000/2001	
Scenario	**Payer**	**Spending**	**Savings**	**Spending**	**Savings**	**Spending**	**Savings**
Actual Cost	Public	$5,876,000		$6,243,000		$7,631,000	
	Private	$9,182,000		$9,711,000		$11,261,000	
Option 1: Mandated Generic Discount Only	Public	$5,737,000	$139,000	$6,115,000	$128,000	$7,553,000	$78,000
	Private	$8,980,000	$203,000	$9,525,000	$186,000	$11,150,000	$111,000
Option 2: Generic Sub at Actual Cost	Public	$5,327,000	$549,000	$5,796,000	$447,000	$7,519,000	$112,000
	Private	$8,440,000	$742,000	$9,222,000	$489,000	$10,806,000	$455,000
Option 3: Mandated Generic Discount with Generic Sub	Public	$4,628,000	$1,248,000	$5,353,000	$890,000	$7,136,000	$495,000
	Private	$7,409,000	$1,773,000	$8,381,000	$1,331,000	$10,194,000	$1,067,000
Option 4: Approximate Reference Pricing at Actual Cost	Public	$4,124,000	$1,752,000	$4,764,000	$1,478,000	$5,470,000	$2,161,000
	Private	$6,529,000	$2,653,000	$7,530,000	$2,182,000	$8,287,000	$2,973,000
Option 5: Approximate Reference Pricing with Mandated Generic Discount	Public	$3,548,000	$2,328,000	$3,929,000	$2,313,000	$4,877,000	$2,754,000
	Private	$5,717,000	$3,465,000	$6,232,000	$3,480,000	$7,199,000	$4,062,000

The policy that encourages generic substitution without the required price reduction resulted in more significant savings than the policy of generic discounts alone.

Option 2 in Table 11, depicts a policy of encouraged generic substitution without requiring generics to have a price reduction. This produces more significant savings at prevailing prices than the policy of generic discounts alone. The savings from a policy that achieved universal generic use (where available) at prevailing generic prices would have saved the Manitoba government $549,000 in 1998/99, $447,000 in 1999/2000, and $112,000 in 2000/01. Savings for private purchasers were $742,000, $489,000, and $455,000 respectively. As with the simulation above, the reduction in potential savings is due to the removal of generic enalapril from the market.

The combined savings over the three years of simulation, under the generic discount and substitution policy for the Manitoba government, would have been $2.62 million.

The combination of generic price discounts and encouraged generic substitution produces significant increases in savings over the application of either policy in isolation. The savings from a policy that achieved generic use (where available) at a minimum of 30% over prevailing brand name prices would have saved the Manitoba government approximately $1.24 million in 1998/99, $0.89 million in 1999/2000, and $0.49 million in 2000/01. Private purchasers would have saved approximately $1.77 million in 1998/99, $1.33 million in 1999/2000, and $1.07 million in 2000/01. Once

again, declining savings are the result of the removal of generic versions of enalapril products.

Therapeutic Interchange: Policies of therapeutic interchange ensure that the availability of a generic version of one product among a category of closely related drugs produces competitive pricing or rational choice among all products within the category.

The first policy scenario designed to simulate competitive pricing between patented and non-patented ACEI products is based on a reference pricing policy, where the reference cost is determined on the basis of cost per day supplied. The reference price in this simulation is approximately 88 cents per day, equivalent to the generic cost of several dosage forms of enalapril (when available), and generic captopril in other periods. This reference price is not the lowest cost per day supplied, because such a cost could reflect the relatively lower cost of therapy for patients requiring low doses. The decision to chose a slightly higher reference price is based on the model implemented in British Columbia.

Under the simulation described here, any patient who had diabetes (with or without nephropathy), or asthma, or had a cardiologist or pulmonary specialist visit were considered exempt from the policy. The simulation holds the utilization patterns for these "exempt" patients at the patterns and levels that actually occurred during the period of analysis. The cost (but not choice) of the drugs used by these individuals was, however, altered under the policy scenario that includes policies to encourage increased savings from generic drugs.

The combined savings over the three years of simulation under the Therapeutic Interchange Policy, for the Manitoba government, would have been $5.39 million. For the private purchasers it would have resulted in a savings of $7.8 million.

Under a policy that established a reference price for ACEI products at prevailing costs of both brand and generics in Manitoba, the Manitoba government would have saved approximately $1.75 million in 1998/99, $1.48 million in 1999/2000, and $2.16 million in 2000/01. Private purchasers would save approximately $2.65 million in 1998/99, $2.18 million in 1999/2000, and $2.97 million in 2000/01.

It is noteworthy that the removal of generic enalapril from the market does not have the same effect on this simulation as it did on the previous policies that affected generic use only. This is because therapeutic interchange policies ensure that those who would use brand name enalapril products consider using generic versions of captopril or lisinopril instead. This, in turn, may place competitive pressures on the manufactures of enalapril products, inducing them to match the price of the off-patent captopril and lisinopril products. By contrast, generic substitution policies on their own will not encourage would-be enalapril users to consider generic versions of any other ACEI drugs.

Savings are further increased when the reference pricing policy is combined with the generic discounts. With the combination of the two policies, the Manitoba government could have saved $7.38 million over the three years of simulation.

When the reference pricing policy is combined with policies to encourage generic discounts, the savings are further increased. Under this combined policy scenario, the Manitoba government would have saved approximately $2.32 million in 1998/99, $2.31 million in 1999/2000, and $2.75 million in 2000/01. Private purchasers would save approximately $3.47 million in 1998/99, $3.48 million in 1999/2000, and $4.06 million in 2000/01.

2.11 Findings: A2RA Step-Up Policy Scenarios

The final simulated policies are those that would encourage first-line use of ACEI drugs for individuals who have been prescribed A2RA. This analysis pertains to new-users, that is to all individuals who have received neither ACEI or A2RA drugs in the prior two years. As with the analysis above, individuals were exempted from the policy scenario if they had diabetes, asthma, or were receiving care from a cardiologist or pulmonary specialist. The number of patients with such morbidities is listed in Table 12. Approximately 13% of new users of A2RA drugs in 1998/99 had coexisting morbidities that would have rendered them exempt under the policy scenario. For these patients, utilization patterns are held constant in the simulation below. In 1999/2000 and 2000/01, approximately 14% and 12% of new users of A2RA drugs, respectively, had morbidities that would render them exempt from the simulated policy change.

Table 12: Patients qualifying for morbidity exemptions under the step-up policy scenario, 1998/99-2000/01

	1998/1999	1999/2000	2000/2001
Exempt	800	1,340	1,210
Non-Exempt	5,340	8,180	8,520
% Exempt	13%	14%	12%

Furthermore, it is assumed that approximately 18% of those individuals who were required to try ACEI products will eventually switch to A2RA drugs. This rate of switching is over twice the estimated 7.9% of ACE who would have dry cough provoking a product switch. The generous estimate of the rate or "stepping-up" puts a conservative bias on our cost savings estimates.

Table 13: Policy simulation: Annual costs per new user of A2RA drugs, 1998/99-2000/01

	1998/1999	1999/2000	2000/2001
Status Quo	$503,031	$789,256	$794,727
Step-Up Alone	$403,453	$609,270	$627,091
Savings	-$99,578	-$179,986	-$167,636
Step-Up With Referenced ACEIs	$302,140	$497,720	$502,151
Savings	-$200,891	-$291,536	-$292,576

In 1998/99, approximately 8,800 patients received a first prescription for either and ACEI or A2RA drug. The rate of new use in Manitoba increased to approximately 12,400 in 2000/01. The total expenditure on drugs consumed by these new users was approximately $2.4 million in 1998/99, $2.83 million in 1999/2000, and $3.2 million in 2000/01.

The percentage of these new users that were prescribed A2RA drugs as a first-line treatment rose from 21% in 1998/99 to 28% in 1999/2000, and declined to 24% in 2000/01. (The decline in 2000/01 may be due to the increased use of the ACEI, ramipril, following the publication of the HOPE trial—see discussion above). The total expenditure on drugs consumed by new users of A2RA drugs was approximately $503,000 in 1998/99, $790,000 in 1999/2000, and $795,000 in 2000/01.

The combined savings of the A2RA Step-Up policy over the three years of simulation would be $735,000.

We simulated two possible policy scenarios to control the level of first-line A2RA drugs use, and thereby control the cost of ACEI or A2RA therapy. The first scenario is a policy requiring that those without relevant complications use an ACEI product before being eligible to use an A2RA drug. Under this simulation, the utilization pattern of those who are non-exempt was altered; these users were "converted" to ACEI users for their first prescriptions and those that followed in later quartets. Persistence on either ACEI or A2RA therapy (including patients who switch from one therapy type to another) was assumed to be 80% within the first year of drug use. The total savings from such a policy would accumulate year after year, as patients who persist on lower cost therapy generate implied savings over time. The annual rate of increased savings from such a policy would reach over $150,000 per year as of 2000/01. The combined savings over the three years of simulation would be $735,000.

The annual rate of increased savings from the combined Step-Up and Therapeutic Interchange policies would reach almost $300,000 per year as of 2000/01.

The second policy simulated here is one that combines the step-up policy for the A2RA class, with therapeutic interchange and generic pricing policies in the ACEI class. This policy will produce additional savings per would-be first-line A2RA user, as those who are successfully started on ACEI drugs would be receiving treatment at substantially lower cost than in the current status for Manitoba. Once again, the step-up policy produces a "rate" of savings that applies year after year for those patients who persist with therapy. The annual rate of increased savings from the combined policies would reach almost $300,000 per year as of 2000/01. Assuming an 80% persistence rate on therapies, the combined savings over the three years of simulation would be $1.3 million.

Although the savings from the step-up policy may be considered modest by comparison to saving generated through the generic substitution policy or the therapeutic interchange policy, the step-up policy may play an important role in the implementation of the latter. If a generic substitution policy or,

Cost-control in one class of drugs might generate cost-inflation in another, i.e. a therapeutic interchange policy implemented on the ACEI product class could result in the market promoting A2RA drugs as first-line treatments.

in particular, a therapeutic interchange policy were to be implemented on the ACEI product class, there is a risk that the market would respond by promoting A2RA drugs as a first-line treatment. As mentioned above, leading manufactures have products in both classes. To the extent that profitability of ACEI products is reduced through policies that are targeted at competitive dynamics within that class, simple economics predicts that firms would promote A2RA drugs more heavily. Consequently, cost-control in one class might generate cost-inflation in another. Experience in British Columbia illustrates that stop-gaps can be put in place. When B.C. put its reference drug program in place on A2RA drugs for ulcer treatment, it also implemented a special authority process for Proton Pump Inhibitors. The combination of policies prevented unintended substations toward the more costly product class (the PPIs).

3.0 DISCUSSION

The classes of ACEI and A2RA drugs are very important from a therapeutic perspective, offering effective management of hypertension and other conditions. Therapeutic similarities amongst products within these product categories would, in a marketplace for ordinary goods and services, lead to significant price competition and steadily falling costs of treatment. One would expect, for example, that prices of patented and non-patented ACEI drug products would be steadily declining due to the effects of generic competition. Similarly, given that the ACEI and A2RA drug classes are very closely related, it would be expected that the use of A2RA drugs would be reserved for only those patients who have tried and failed on ACEI drugs or that manufacturers of A2RA drugs would charge prices that are competitive with both brand and generic ACEI products. Actual pricing and utilization patterns do not reflect these efficiencies. The pricing and utilization patterns revealed in this study indicate that the competitiveness of firms and the cost-sensitivity of consumers within and across the ACEI and A2RA drug categories could be improved.

Patterns revealed in this study indicate that competition between firms and cost-sensitivity of consumers could be improved within and across the ACEI and A2RA drug categories.

To illustrate the potential to achieve competitive pricing among patented and non-patented drug products, together with cost-conscious product selection by patients/prescribers, we simulated multiple stages of policy intervention for the ACEI and A2RA drug classes. Each of these policy simulations builds in logical sequence, starting with the promotion of competitive pricing and price-conscious product selection as it pertains to off-patent ACEI products. Onto this baseline, "therapeutic interchange" policies are added that would promote consumers' price sensitivity when selecting among both patented and non-patented products. Finally, a "step-up" policy to encourage first-line use of ACEI products is added to these simulations.

The results of this analysis illustrate that generic pricing and substitution policies are a necessary first step if Manitoba is to realize the potential benefits of improved pricing and product selection in these classes. Generic substitution policies on their own produce between $1.5 and $2 million in savings within the ACEI category of drugs alone, representing over 10% of total spending in this category. Such policies have been implemented for all multi-source product categories in other provinces. Consequently, Manitoba can look to Ontario, Alberta, British Columbia and other jurisdictions for guidance regarding how to implement, and perhaps improve upon, programs to negotiate lower generic prices while encouraging their use when available. For example, combining generic substitution and negotiated generic price cuts through a tendering process may be an attractive policy option insofar as it can produce savings through cooperation with manufacturers.

Generic pricing and substitution policies are a necessary first step if Manitoba is to realize the potential benefits of improving pricing and product selection in these classes.

Savings of as much as $5 to $7 million annually, in Manitoba, could be achieved by implementing therapeutic interchange policies for ACEI drug products. Potential savings must be weighed against their potential to provoke negative responses.

After generic pricing policies have secured competition between competing versions of non-patented drugs, policymakers might consider "therapeutic interchange" and "step-up" programs. Therapeutic interchange policies for ACEI drug products could generate as much as $5 to $7 million in annual savings in Manitoba. A step-up policy requiring that ACEI products be tried prior to the use of A2RA drugs could generate an additional $250,000 or more in savings. Though the "savings" generated by the step-up policy appear small, its implementation might be necessary if a therapeutic interchange policy is to be used on ACEI drug products. The step-up policy would avoid the potential side effect that a therapeutic interchange policy on ACEI products may promote the first-line prescribing of A2RA drugs.

The potential savings generated by therapeutic interchange policies or prescribing protocols must be weighed against their potential to provoke negative response. Retailers represent a potential political opponent to implementing policies that will reduce the cost of generic drugs while strongly encouraging their use because lowering ingredient costs per prescription dispensed reduces the scale of potential retail mark-ups, thereby reducing profits to the retailer. However, while retailers may oppose programs aimed at generic substitution policies, this potential political conflict may be more easily managed than conflict with brand name drug manufacturers over a policy of therapeutic interchange.

Lower dispensing fees in Manitoba may be an indication that Manitoba pharmacies earn a greater share of their net revenues from mark-ups on drug ingredients.

Based on figures collected by the Canadian Pharmacists Association (CPhA, 2002), Manitoban pharmacies charge the lowest average fee per regular prescription dispensed in 2001 (See Table 14). The reported average fee charged in Manitoba was $6.01. This is 14% lower than the average of $6.96 for the ACEI and A2RA prescriptions dispensed in 2001 as analyzed in this report. Nonetheless, the reported professional fee of $6.01 for Manitoban pharmacists is 11% below the average $6.79 professional fee charge in other provinces recorded in the Canadian Pharmacists Association report. A fee disparity with Ontario, Alberta and British Columbia might be rationalized on the basis of differences in average commercial real estate costs. However, that dispensing fees are lower in Manitoba than in so many other provinces may be an indication that Manitoban pharmacies earn a greater share of their net revenues from mark-ups on drug ingredient costs. Consequently, policymakers may wish to consider means of allowing increases in professional fees while introducing policies to encourage generic price discounts and substitution. Every $1.00 increase in dispensing fees (which represents 16% of reported fees) would represent only a 2% increase in the total cost of ACEI and A2RA drugs dispensed in Manitoba. Consequently, the estimated savings from reduced generic prices and increase generic use would far outweigh the cost of a significant increase in professional fees paid to Manitoban pharmacists.

Table 14: Average professional fee charged for regular prescriptions, by province, 2001

Province/Territory	Average Professional Fee (2001)
British Columbia	6.61
Alberta	--
Saskatchewan	6.19
Manitoba	6.01
Ontario	6.47
Quebec	6.97
New Brunswick	7.68
Nova Scotia	7.68
Prince Edward Island	7.45
Newfoundland	--

-- = average not available

Evidence in B.C. where a therapeutic interchange policy was applied, indicate that manufacturers are coming to accept such policies are an effective manner of increasing price sensitivity among consumers, without altering overall access to the products that are on the market.

A therapeutic interchange policy might provoke a more challenging reaction from pharmaceutical manufacturers. The majority of every dollar saved in ingredient spent on ACEI or A2RA drugs is lost income to a concentrated few manufactures of these products. Such losses may not be taken lightly. The experience of British Columbia illustrates. British Columbia's therapeutic interchange policy for ACEI drugs, which took the form of reference based pricing, provoked a considerable backlash from drug manufacturers in 1997. Major lawsuits, negative public relations campaigns, and threats to reduce research investment, all made by manufacturers of ACEI products, were sufficient grounds for the B.C. government to freeze all plans of expanding therapeutic interchange to other classes. In July 2003, however, B.C. did expand the program to include the class of proton pump inhibitors (drugs used to treat ulcers and gastroesophageal reflux disease). The recent application of the therapeutic interchange policy in B.C., combined with an absence (to date) of organized backlash from manufactures, might indicate that manufactures are coming to accept that such policies are an effective manner of increasing price sensitivity among consumers without altering overall access to the products that are on the market.

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APPENDIX A: CROSS TABULATIONS OF PATIENT COSTS

As mentioned in the introduction to this report, cost growth is a significant motivation for public subsidy of drug costs, and also a threat to the programs that provide such subsidy. The analysis conducted here characterizes cost-dynamics and potential savings from alternative policy approaches that would accrue to both private and public payers for the specific classes of drugs being investigated. Given the new interest in catastrophic drug coverage following release of the Romanow Report, we review the scale, concentration and persistence of the private and public cost of these drugs among individuals within the Manitoba population. We contrast the ongoing pattern of private and public cost for ACEI and A2RA drugs against the concentration and persistence of private and public expenditures on all prescription drugs for individuals within Manitoba. This unique analysis provides some indication of what could be deemed a "catastrophic creep"—a gradual increase in the percentage of individuals whose drug costs could be considered "catastrophic" based on a fixed or even inflation adjusted threshold. The growth in the use and cost of ACEI and A2RA drugs may be an example of one force pushing up the rates of "high-cost" drug use in the population.

Methods

The cross tabulations computed for our analysis are based on the total drug expenditures by each individual during the year, whether the spending came from public or private sources. We assigned individuals into 20 groups, each corresponding to a five-percentage point band of the distribution of total drug costs (both private and public). Persons in the 19th band of 20 had high drug expenditures, and were in the 91st to 95th percentile in a given year based on their total drug expenditures. Those in bands 11 to 20 comprise the top 50% of Manitobans in terms of drug spending. And so forth.

Each cross tabulation is presented in a matrix of probabilities, sometimes referred to as a transition matrix. Each row of the matrix corresponds to the relative level of drug expenditures that individuals accumulated during the base year of analysis. The columns represent the relative level of expenditure that the individuals had during the end year of the analysis. The cell of the matrix that lies in the Rth row and the Cth column represents the number (or percentage) of individuals that were in the Rth group in terms of base year total drug costs and then in the Cth group during the end year.

Cross tabulations were created to depict changes in an individuals' relative expenditure of drugs from year to year, and from the overall base year (1995/96) though to the overall end year of the analysis (2000/01). The

cohort used for the analysis of the concentration of spending among individuals was comprised of anyone who used one or more prescription for any drug over the entire period. This will under sample non-users of pharmaceuticals and therefore under sample the relatively young, especially young men. No adjustment was made for individuals who died or were admitted to hospital during the period of analysis; rather, these individuals will appear as ones who had zero expenditures in a given year. This will under report the rate of persistence among high drug users, since seriously ill Manitobans who died or were admitted to hospital will appear to have had a sudden drop in expenditures.

Findings

The persistence and concentration of spending for all prescription drugs among Manitobans is depicted in the three transition matrices found in Appendix Table 1. The sample for this analysis included all (1.169 million) Manitobans who used one or more prescriptions during the period of 1995/96 through to 2000/01. The sample is divided into 20 equal sized five-percentile wide bands according to the level of each individual's prescription drug expenditures in the year.

The left hand column of each matrix within Appendix Table 1 lists the average level of spending for individuals within the five-percentile wide bands of the population during 1995/96. This shows that the 35% of the sample population with the lowest level of spending in 1995/96 (labelled "<35") had no drug expenditures in that year. Similarly, individuals at the median of the sample, the 50 group, incurred an average of only $24 in drug costs. Expenditures per individual increase exponentially up the distribution beyond the median. It is striking that the top 5% of the sample population had an average drug expenditure of $1,610 in 1995/96. The individuals in this sub-group of the sample population account for half of the total expenditures on prescription drugs in Manitoba in that year.

The top row of the three tables lists the average level of spending for individuals within the five-percentile wide bands of the population during 1996/97, 1998/99 and 2000/01 respectively. In all of these years, the 35% of the sample population with the lowest level of spending had no drug expenditures at all. The median level of drug expenditures among the sample population was approximately $23, $27, and $36 the respective years. Thus, the "expenditure inflation rate" for the half of the population that has very modest drug costs in a given year was 50% over the five years between 1995/96 ($24) and 2000/01 ($36). This contrasts with 75% expenditure growth among the top 5% of the sample population over the same period. Average drug expenditures among the top 5% of the sample population were $1,661 in 1996/97, $2,091 in 1998/99, and $2,811 in 2000/01. In

each of the years, these high-users accounted for approximately half of the total expenditures on prescription drugs in Manitoba.

The percentage figures within the table report the proportion of the group that fell within a given 1995/96 five percentile band corresponding to the row of the data that ended up in the end-year five percentile band corresponding to respective column of the data. The table defines the end-year: 1996/97, 1998/99, or 2000/01. The far right columns of data summarizes broad bands of percentiles that individuals may land in; specifically, it lists the percentage of the 1995/96 five-percentile cohort that ended up with expenditures in the top half, top quarter, or top 10% of the distribution of spending in the end-year. These figures give broad indications of persistence of spending.

From each table, it can be seen that a minority of individuals who began with spending below the median in 1995/96 would end up with expenditures above the median in any of the following years. Those who are relatively healthy stay relatively healthy. A very small fraction (approximately 3%) of these individuals would make the transition into the top 10% of users in any of the end-years. The persistence of low levels of drug expenditures is mirrored by persistence in high levels of drug use. Notably, a majority of individuals in the top 5% of users in 1995/96 remained in the top five or 10% of users in 1996/97, 1998/99, and 2000/01. Even after five years, 80% of those in the top 5% of users in 1995/96 continued to have expenditures that put them in the top quarter of the population sample.

Appendix Table 1: Drug expenditure transition matrices from 1995-1996, 1995-1998, 1995-2000

Percentile 95 to Percentile 96

	$$	$0	$6	$11	$16	$23	$32	$45	$64	$94	$140	$211	$342	$606	$1,661	$322	$592	$1,133
$$		<35	35	40	45	50	55	60	65	70	75	80	85	90	95	50+	75+	90+
$0	<35	82%	0%	0%	0%	0%	4%	4%	3%	2%	1%	1%	1%	1%	1%	18%	5%	1%
$7	35	46%	0%	0%	0%	0%	4%	4%	3%	2%	1%	1%	1%	1%	1%	17%	5%	1%
$12	40	44%	37%	0%	0%	0%	4%	4%	3%	2%	1%	1%	1%	1%	1%	19%	5%	1%
$17	45	41%	63%	19%	0%	0%	4%	4%	3%	2%	1%	1%	1%	1%	1%	18%	5%	1%
$24	50	35%	0%	81%	0%	0%	4%	4%	3%	2%	2%	1%	1%	1%	1%	19%	5%	1%
$33	55	30%	0%	0%	81%	0%	3%	5%	3%	2%	2%	1%	1%	1%	1%	19%	5%	1%
$45	60	25%	0%	0%	19%	36%	6%	8%	6%	4%	4%	4%	4%	5%	3%	81%	21%	8%
$63	65	19%	0%	0%	0%	39%	5%	10%	11%	8%	7%	6%	6%	6%	3%	100%	27%	9%
$91	70	15%	0%	0%	0%	23%	3%	9%	15%	14%	10%	8%	7%	7%	4%	100%	36%	11%
$137	75	9%	0%	0%	0%	3%	11%	6%	8%	15%	17%	15%	11%	7%	4%	100%	56%	12%
$207	80	0%	0%	0%	0%	0%	8%	4%	6%	12%	16%	22%	16%	11%	5%	100%	70%	16%
$340	85	0%	0%	0%	0%	0%	6%	4%	5%	8%	14%	15%	23%	17%	7%	100%	77%	24%
$617	90	0%	0%	0%	0%	0%	7%	4%	6%	7%	9%	11%	16%	26%	14%	100%	75%	40%
$1,610	95	0%	0%	0%	0%	0%	9%	4%	4%	5%	5%	5%	6%	12%	51%	100%	78%	63%
		35%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	50%	25%	10%

Percentile 95 to Percentile 98

	$$	$0	$8	$12	$18	$27	$38	$53	$77	$114	$172	$266	$445	$779	$2,091	$406	$751	$1,435
$$		<35	35	40	45	50	55	60	65	70	75	80	85	90	95	50+	75+	90+
$0	<35	55%	6%	4%	5%	6%	5%	4%	3%	3%	2%	2%	2%	2%	1%	31%	9%	3%
$7	35	50%	6%	5%	5%	6%	5%	5%	4%	3%	3%	3%	2%	2%	1%	34%	11%	3%
$12	40	47%	8%	7%	5%	6%	5%	5%	4%	3%	3%	3%	2%	2%	1%	34%	11%	3%
$17	45	44%	8%	7%	5%	6%	6%	5%	4%	4%	3%	3%	3%	2%	1%	36%	12%	3%
$24	50	40%	8%	8%	5%	6%	6%	5%	5%	4%	4%	3%	3%	2%	1%	39%	14%	4%
$33	55	35%	8%	9%	5%	6%	6%	6%	5%	5%	4%	4%	3%	3%	1%	43%	16%	4%
$45	60	29%	7%	9%	5%	6%	6%	6%	6%	6%	6%	5%	4%	3%	2%	49%	19%	5%
$63	65	23%	6%	9%	5%	5%	6%	7%	7%	7%	7%	6%	5%	4%	2%	57%	24%	6%
$91	70	16%	4%	7%	6%	5%	6%	7%	9%	9%	9%	7%	6%	5%	3%	66%	30%	8%
$137	75	11%	3%	5%	6%	4%	5%	7%	10%	11%	11%	10%	8%	7%	3%	76%	39%	10%
$207	80	7%	1%	3%	6%	3%	4%	6%	9%	11%	13%	12%	11%	9%	5%	83%	50%	13%
$340	85	5%	1%	1%	5%	3%	3%	5%	7%	9%	11%	14%	15%	13%	9%	88%	62%	22%
$617	90	4%	0%	0%	5%	2%	3%	4%	5%	6%	7%	11%	16%	19%	18%	91%	72%	38%
$1,610	95	3%	0%	0%	4%	2%	2%	2%	2%	3%	3%	6%	9%	18%	46%	93%	81%	64%
		35%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	50%	25%	10%

Percentile 95 to Percentile 00

	$$	$0	$10	$16	$25	$36	$52	$74	$109	$162	$242	$386	$625	$1,052	$2,811	$555	$1,023	$1,932
$$		<35	35	40	45	50	55	60	65	70	75	80	85	90	95	50+	75+	90+
$0	<35	42%	9%	8%	7%	6%	5%	4%	4%	3%	3%	3%	2%	2%	1%	33%	11%	3%
$7	35	62%	3%	3%	4%	4%	4%	4%	3%	3%	3%	2%	2%	2%	1%	28%	11%	3%
$12	40	59%	3%	4%	4%	4%	4%	4%	4%	3%	3%	3%	2%	2%	1%	30%	11%	3%
$17	45	55%	3%	4%	4%	4%	4%	4%	4%	4%	3%	3%	3%	2%	1%	33%	13%	3%
$24	50	50%	3%	4%	5%	5%	5%	5%	5%	4%	4%	3%	3%	2%	1%	38%	14%	4%
$33	55	44%	4%	4%	5%	6%	6%	6%	5%	5%	5%	4%	4%	3%	2%	43%	16%	4%
$45	60	37%	3%	4%	5%	6%	6%	7%	6%	6%	5%	5%	4%	3%	2%	50%	19%	5%
$63	65	30%	3%	4%	5%	7%	7%	8%	7%	7%	6%	6%	5%	4%	2%	58%	23%	6%
$91	70	22%	3%	4%	5%	7%	7%	8%	8%	8%	8%	8%	7%	6%	5%	67%	28%	7%
$137	75	15%	2%	3%	4%	6%	7%	8%	9%	10%	9%	9%	7%	6%	3%	76%	35%	9%
$207	80	11%	2%	2%	3%	5%	6%	7%	8%	10%	11%	11%	10%	8%	5%	81%	45%	13%
$340	85	9%	2%	2%	2%	3%	5%	5%	6%	8%	10%	13%	14%	12%	9%	85%	58%	21%
$617	90	7%	1%	2%	2%	2%	3%	4%	4%	6%	7%	11%	14%	18%	18%	88%	69%	36%
$1,610	95	7%	1%	1%	1%	1%	2%	2%	2%	3%	4%	5%	8%	19%	44%	90%	80%	63%
		35%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	50%	25%	10%