

# Why is calling an ACE an ACE so controversial? Evaluating reference-based pricing in British Columbia

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**I**s an angiotensin-converting-enzyme (ACE) inhibitor an ACE inhibitor regardless of which of the numerous drug manufacturers, generic or branded, makes and markets the drug? Such a question may seem facile, but the answer is extremely important — for if it is Yes, it would be possible to prescribe ACE inhibitors generically. The answer to the question requires analyses of the evidence from clinical trials or evidence from longitudinal databases with long-term follow-up, using the appropriate methods of systematic review. To date, however, no such systematic review has been published.

At a more fundamental level, there have been no randomized comparative studies comparing one ACE inhibitor with another for the treatment of hypertension. Thus, although all ACE inhibitors have been shown to reduce blood pressure to a comparable degree, they have different dosage schedules and may have different side-effect profiles. Thus, it may well be that compliance with treatment and use of medical services varies with the particular ACE inhibitor prescribed. One way to try to assess such effects is to use population-based data available from government prescription drug programs.

Some studies have looked at whether one class of antihypertensives is better than another as start-up (initial) therapy,<sup>1</sup> whereas others have evaluated switching between ACE inhibitors.<sup>2</sup> The latter study showed that patients with hypertension who received an initial prescription for the ACE inhibitor captopril used health care services more than those whose initial prescription was for enalapril or lisinopril. However, the pharmacokinetic properties of captopril differ from those of other ACE inhibitors, and thus there may have been systematic differences (in terms of blood pressure, coexisting illnesses or severity of illness) between patients who received this drug initially and those who received one of the other drugs. For example, in patients with unstable or labile blood pressure, physicians may use an ACE inhibitor with a more rapid onset and shorter elimination half-life for easier titration, such as captopril.

In 1996 Pharmacare, the provincial drug plan in British Columbia, introduced reference-based pricing. In doing so, it essentially imposed a form of therapeutic substitution that assured prescribers that the answer to the question posed at the beginning of this article was affirmative — that all ACE inhibitors are equivalent. But was the program correct in giving this assurance? Five years later, the first

evaluation of this policy of therapeutic substitution is being published (see page 737).<sup>3</sup>

Among other findings, Schneeweiss and associates<sup>3</sup> have shown that reference-based pricing had a differential effect according to income level on the switching behaviour of eligible beneficiaries who were taking an ACE inhibitor that was no longer fully reimbursed by Pharmacare. Among the 48 355 patients who were receiving an ACE inhibitor before the introduction of reference-based pricing that was not fully covered afterward, 44% opted to stay on the same medication and pay the difference in costs, 31% were given exemptions from switching, 18% switched to one of the no-cost ACE inhibitors (captopril, quinapril or ramipril), 4% switched to another antihypertensive, and 3% stopped taking all antihypertensives.

Because some patients are willing to pay out-of-pocket to cover the difference in cost between their existing ACE inhibitor (a cost-shared drug in the new reference-based pricing system) and the no-cost drugs (“referenced” drugs in the reference-based pricing system), there are economic implications of deciding not to switch. Out-of-pocket payments are in essence a form of copayment, and copayments are known to affect demand for health care in health insurance settings that are based on user fees.<sup>4</sup>

Copayments have 2 classes of effect, which economists refer to as substitution and income effects. The overall impact of copayments is to reduce consumption of the item of interest, because something that was previously available free of charge (in this case, the cost-shared drug) now involves a cost to the patient, although the reference drug (or drugs) is still free to the patient. Hence the relative price of the cost-shared drug increases and its consumption can be expected to fall. This is known as the substitution effect. In addition, because expenditures on cost-shared drugs reduce the amount of income available for other goods, regardless of income level, less overall income is available to be spent on any good or service. This is known as the income effect.

A decrease in the use of cost-shared ACE inhibitors, which occurred to a greater extent among low-income patients than among higher-income patients, is not as significant as the substantial decline (11%) in consumption of all ACE inhibitors. In other words, reference-based pricing affected demand in a manner that led to an 11% decline in the use of ACE inhibitors. Furthermore, it also caused a 10% decline in the use of all antihypertensives. Since it is

already well known that hypertension is undertreated,<sup>5</sup> further declines in drug use by patients with hypertension is not good news. A more in-depth investigation of these effects is urgently needed.

The role of patient income levels, although extremely important, cannot be inferred from the analysis of Schneeweiss and associates.<sup>3</sup> This is so both because the entire range of income levels was very low and extremely compressed and because the estimated odds ratios were not consistent across income levels and switching categories.

Under reference-based pricing, people eligible for Pharmacare benefits can avoid being switched to one of the reference ACE inhibitors if they qualify under certain exemptions. These patients must therefore be excluded from the analysis. Schneeweiss and associates<sup>3</sup> have attempted to do so by analyzing patients with exemptions as a separate group. However, given the number of different ways in which a person can qualify for an exemption and the nature of the administrative claims database used as the data source for the analysis, patients with exemptions cannot be identified with much accuracy, nor can the reason for exemptions be verified.

In Canada, we have a “near-universal” system of coverage for health care interventions and services, except for outpatient prescription pharmaceuticals. This anomaly has led to a patchwork of mostly provincial drug plans that attempt to fill this gap in the universality of Canadian medicare.<sup>6</sup> Yet as the crisis in health care funding deepens, it is this very underprovided aspect of Canadian medicare that gets targeted for cost control.

Policy-makers inevitably fail to recognize that the substitution effect will cause offsetting changes in the use of

other health care interventions that are not being targeted. Even worse, as the evidence presented by Schneeweiss and associates seems to suggest, we may see a decline in overall use without concomitant increases in other interventions that might have comparable effects in reducing hypertension. If so, we can only speculate as to the long-term effects of such policies on the health outcomes of Canadians.

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