and catapulted out of life-patterns that had endured for thousands of years."[6]

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A worthy Web site

I recently underwent a set of screening, then diagnostic, mammograms, followed by 2 ultrasounds and a biopsy. I found trying to gather reliable and comprehensive information about breast health issues by phone, in person and online to be an exercise in sleuthing and perseverance — until I came across the *CMAJ* Web site (www.cma.ca/cmaj), which is offered at no subscription cost. It provided a clear, concise and complete guide to all of the questions to which I needed answers in order to be informed at each stage of the screening and diagnosis process.

Thank you for providing an informative and helpful online resource to both health care practitioners and lay people.

E. Jill Watson
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Anticoagulant prophylaxis against stroke

Jaime Caro and colleagues are to be congratulated for their study confirming the beneficial effect of anticoagulants to prevent stroke in atrial fibrillation.[1] In the same issue Stuart Connolly asks why so many eligible patients are not receiving anticoagulant therapy.[2] I would suggest the following possible reasons.

First, patients may be reluctant to go to a testing laboratory on a regular basis. They may also be concerned about the restrictions the use of blood thinners may impose on their lifestyle.

Second, there is the issue of informed consent. Using the results of the study by Caro and colleagues, a diligent physician might explain to a patient that the risk of stroke in individuals taking warfarin is 2.3 per 100 person-years as opposed to 6.7 per 100 person-years in the no-treatment group and that the hazard rate from bleeding is 3.4 per 100 person-years in the warfarin group versus 1.9 per 100 person-years in the no-treatment group. The patient might assume that taking warfarin would mean going from the frying pan into the fire.

The third reason is physician reluctance. Connolly makes no mention of the increased workload anticoagulant therapy places on the treating physician and his or her staff. Whenever a patient goes for a blood test, the international normalized ratio (INR) results are typically phoned into the physician's office. The physician must then modify the dose as required and notify the patient of any changes. This requires several phone calls and can be a major source of anxiety (and possible medicolegal liability) when, for whatever reason, the doctor's office is unable to reach the patient to make the required medication changes. Admittedly, in BC physicians do get paid the princely sum of $2.73 for providing this service.

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Reference-based pricing

We found the articles by Lutchmie Narine and colleagues[1] and Chantal Bourgault and associates[2] to be of particular interest, as we have been involved in the development of the Reference Drug Program in BC from its inception. The program has received both criticism and accolades since it was launched in the fall of 1995. Criticism has come primarily from the pharmaceutical industry, as any savings that governments achieve from the application of the policy are also reduced profits for the drug companies. Indeed, it has been stated that one gauge of any policy's effectiveness is the vigour of the industry response.[3] Accolades have come from those who recognize the importance of a sustainable drug program for the long term.

Narine and colleagues[1] attempt to draw correlations between the reference pricing policies in Europe and those in BC. Although there may be some similarities, there are significant differences. The primary focus of the policy in BC is the baseline prescribing habits of physicians. The policy is designed to ensure that the most cost-effective agent within a drug class is used initially. If there are particular patient circumstances that would justify the use of a more costly agent, such as an adverse reaction or lack of therapeutic effect, the alternative agent is funded fully. In addition, the Reference Drug Program in BC does not target generic equivalents as stated in the article, but rather it targets competing drugs in a class.

Bourgault and associates[2] review the utilization of a select group of angiotensin-converting-enzyme (ACE) inhibitors, as well as hospital admissions and physician visits. Although the authors speculate that there are therapeutic differences among the ACE inhibitors, they present little evidence to support this assertion.

We agree with the critical comments by editorialists Paul Grootendorst and Anne Holbrook.[4] There are many plausible explanations for the differences in health services utilization rates ob-

served. In addition to it being the ACE inhibitor of choice in hypertension at the time, captopril was likely available on all the hospital formularies in the province at the time. As it is unlikely that many hospitals included lisinopril on their formularies in the early 1990s, it is entirely possible that patients in hospital were preferentially prescribed captopril simply because of its availability and therapeutic efficacy.

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In a study of reference-based pricing, Chantal Bourgault and colleagues[1] challenge the therapeutic equivalence of 3 ACE inhibitors on the grounds that patients with hypertension whose treatment was started with captopril had more subsequent hospital admissions and ambulatory medical visits than those who were initially prescribed enalapril or lisinopril.

First, it is unclear why they used an intention-to-treat analysis. What they needed to determine was whether the medication used was the cause of these outcomes. In a recent Canadian study[2] by 3 months 13% of patients with hypertension who were initially prescribed an ACE inhibitor did not persist, and by 4.5 years only 53% were still taking that medication.

Second, before wading into a database analysis to look for correlations, there should surely have been a more precise statement of a clinically plausible hypothesis than, I wonder if all 3 drugs are associated with the same admission rate? These were patients who were starting treatment for uncomplicated hypertension, a condition that is unlikely of itself to be the cause of hospital admissions.

Was the hypothesis then that captopril was less effective in controlling blood pressure, and that this caused a higher incidence of heart disease and stroke in the subsequent 4 years? There is ample evidence that blood pressure control with these 3 agents is fairly comparable, and even if blood pressure was less well controlled, the resultant increase in heart disease and stroke would be unlikely to appear so rapidly.

Or was the hypothesis that with captopril there would be more side effects or drug interactions of sufficient severity to warrant hospital admission? These hospital discharge diagnoses, which were ascertained but not reported, would surely tell us the reason for hospital admission and would suggest the way in which captopril was (or was not) the cause of increased admission rates.

Numerous possible reasons for this result, other than the absence of therapeutic equivalence, are cited in this paper and in an accompanying editorial.[3] The most likely explanation is that the patients initially prescribed captopril were more sick before therapy started than the patients prescribed the other drugs, as evidenced by higher drug use and higher admission rates. Surely one can never say that one has corrected for this, but only that one has tried to correct for this.

I think we should conclude that this is a provocative study that merits clarification, but the conclusion that the result "suggests that ACE inhibitors may not be therapeutically equivalent" is premature.

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[The authors respond:]

One of the ways to move beyond partisan discussion about the BC Reference Drug Program is to begin looking at the objective evidence of the program's effectiveness, as we did in our article.[1] Although we are pleased that our study has drawn interest and comment from those involved in the development of the program, it is unfortunate that the comments were directed at clarifying perceived misstatements that in our view are not present in the article.

Bob Nakagawa and Rick Hudson question our comparison of the BC reference pricing policy with those in Europe, citing differences between the policies. A careful reading of our article will reveal that we are aware of these differences and so did not attempt to make any correlations beyond indicating that jurisdictions in Europe experimented with this form of policy before BC and reporting that as in Europe the initial effect of the BC program has been a decline in annual drug expenditures. We devoted a paragraph to listing how the BC program differed from others, and in particular we indicated the existence of "an option for special authority approval, which provides full coverage for a more expensive drug if the prescribing physician can justify its use."

Nakagawa and Hudson indicate that we stated that the BC program targets generic equivalents. At no point did we make such a statement. If this were so, our analysis and presentation of data would have highlighted generic equivalents. We did indicate in the article that reference-based pricing may be most applicable to a limited segment of the pharmaceutical market that includes therapeutic categories containing generic equivalents. This statement was

made as part of a general discussion about why reference-based pricing policies may not substantially slow the growth of pharmaceutical expenditures in the long term and did not refer to the BC program specifically.

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Bob Nakagawa and Rick Hudson suggest that captopril was the ACE inhibitor of choice in hypertension at the time of our study and that patients in hospitals might have been preferentially prescribed captopril. Our data, however, show that among first-time users of ACE inhibitors, the use of captopril was considerably lower than that of the other 2 agents; this does not indicate preferential use of captopril initially. Moreover, our study included only prescriptions dispensed on an outpatient basis, and availability of the drug on the hospital formularies should not have direct relevance to our study. Thus, we disagree with the claim that we present "little evidence" of the presence of therapeutic differences among ACE inhibitors on that basis.

Maurice McGregor contends that our conclusions are premature. He refers to a study by Caro and colleagues[1] that showed very low rates of persistence with ACE inhibitors in a similar cohort. We agree entirely that one should take such changes in drug use into account when trying to infer causality between drug use and subsequent use of health services, which our study did not. Our intent-to-treat analysis was a first step in using population-level data to assess whether agents belonging to the same therapeutic class differ in respects other than simply their chemical structures, such as the way they are prescribed to different patients and their impact on health services utilization. Additional studies accounting for complex patterns of drug use would be welcome.

Reference-based pricing policies aim to ensure that the more cost-effective medication is used. Although we are advocates of this approach, we believe that such policies should be carefully evaluated, not only in terms of health-related spending but also in terms of population health. McGregor's statement that "this is a provocative study that merits clarification" is certainly true. Indeed, our study had several methodological limitations, as Paul Grootendorst and Anne Holbrook correctly pointed out in an accompanying editorial,[2] and there may be other plausible explanations for the observed differences. However, population-based studies are essential in evaluating whether policies aimed at reducing costs may not in fact increase long-term costs and, more important, negatively affect public health.

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Much ado about Furbies

The research letter by Kok-Swang Tan and Irwin Hinberg regarding the Furby toy[1] raises questions. Was more than 1 Furby tested? There may be variance among Furbies. How did they obtain the Furby? When I tried to get one at Christmas time in 1998, they were virtually impossible to obtain. Did they use expensive AAA batteries, or cheaper ones that might reduce the electric and magnetic fields generated by the Furby? Finally, they state that the electric and magnetic field strengths generated by the Furby were about "70 times weaker" than those from a digital telephone. One time weaker would obviously mean no electromagnetic waves whatsoever, but it is hard to picture something that is 70 times weaker. Does this mean 1/70th, or 70% less? Or do the Furbies actually absorb electromagnetic waves, being in a negative mode?

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Reference

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[One of the authors responds:]

We tested 2 Furbies. Neither caused any effect on medical devices. We had no difficulties in obtaining the Furbies. We obtained one from the Canadian distributor in Montreal and the other from a friend. Many colleagues had offered to lend us their Furbies for testing. We used 4 Energizer alkaline batteries. The voltage of each battery was checked after each test to ensure that it had not fallen below 1.50 V DC (about 94% of the initial voltage). As we pointed out in our paper the electric and magnetic field strengths generated by the Furby were weak — not zero. The term "70 times weaker" means 1/70th the strength.

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Old ways of treating TB may hold new appeal

As a physician who was involved in treating tuberculosis before the introduction of chemotherapeutic drugs, I found the article by Earl Hershfield