study was driven by an excellent medical education campaign supported by a powerful landmark clinical trial. Is it not possible that application of the results of the HOPE trial in diabetic patients and in patients with vascular disease has saved many lives and that it has prevented numerous myocardial infarctions and strokes?

David Fitchett
Terence Donnelly Heart Centre
St. Michael's Hospital
Toronto, Ont.

References

1. Pilote L. Ramipril use in Canada: HOPE or HYPE? [editorial]. *CMAJ* 2003;168(5):568-9.
2. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation (HOPE) Study Investigators. *Lancet* 2000;355:253-9.
3. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med* 2000;342:145-53.
4. Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. *Lancet* 1993;342:821-8.
5. Garg R, Yusuf S. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials. *JAMA* 1995;273:1450-6.
6. Arnold JMO, Yusuf S, Young J, Mathew J, Johnstone D, Avezum A, et al, on behalf of the HOPE Investigators. Prevention of heart failure in patients in the Heart Outcomes Prevention Evaluation (HOPE) study. *Circulation* 2003;107:1284-90.

Competing interests: Dr. Fichett has received speaker fees and travel assistance from Merck, BMS, Aventis and Servier.

A headline appearing in the highlights section of the March 4, 2003, issue of *CMAJ* was "The hype around HOPE," in reference to an article by Karen Tu and colleagues[1] and an accompanying commentary by Louise Pilote.[2] This expression was an appropriate play on words to describe changes in the prescribing of ramipril after publication of results from the large Canadian-led HOPE trial.

Reading these articles prompts questions about physicians' role in patient care. Will we continue to be led, like sheep, deeper and deeper into pharmaceutically driven disease management, or can we take charge by considering the real meaning of population health rooted in prevention?

Ramipril and other drugs are being investigated for their potential in preventing type 2 diabetes. But we already know how to prevent type 2 diabetes: lasting lifestyle change. Exercise and the maintenance of a stable, healthy weight prevent adult-onset diabetes. Let us not forget that 90% of type 2 diabetic patients are overweight, and many are obese — hence the recently coined term "diabesity."

Preventing type 2 diabetes through the use of drugs does not represent a success, nor is it honourable. Rather, it represents an abysmal failure and remains unbecoming of the medical profession, driving up health care costs while fuelling more disease and management research, not to mention the fact that all drugs, including those given for their beneficial effects, also have side effects.

Wally Shishkov
Physician
Guelph, Ont.

References

1. Tu K, Mamdani MM, Jacka RM, Forde NJ, Rothwell DM, Tu JV. The striking effect of the Heart Outcomes Prevention Evaluation (HOPE) on ramipril prescribing in Ontario. *CMAJ* 2003;168(5):553-7.
2. Pilote L. Ramipril use in Canada: HOPE or HYPE? [editorial]. *CMAJ* 2003;168(5):568-9.

Competing interests: None declared.

Louise Pilote[1] implies that physicians who prescribed ramipril to more of their diabetic patients after the results of the HOPE study were publicized did so primarily because of marketing hype rather than solid research evidence. As a clinical epidemiologist and diabetes specialist, I am baffled by this position. The HOPE study[2,3] was by far the largest clinical trial evaluating an ACE inhibitor and enrolled a much broader clinical population than its predecessors. It included a prespecified subgroup of 3577 diabetic participants, possibly more than the total number of diabetic subjects enrolled in all previous ACE inhibitor trials. Diabetic (and nondiabetic) subjects assigned to receive ramipril had statistically and clinically significant risk reductions for major cardiovascular events. Strikingly, the results were homogeneous across all subgroups examined: male and female; with and without previous cardiovascular disease; younger than 65 years of age and 65 years and older; and with and without hypertension, microalbuminuria or dyslipidemia (or any combination of these comorbidities). Therefore, the HOPE study provided excellent evidence to support the use of ramipril in many diabetic patients who would not previously have been considered candidates for an ACE inhibitor. The HOPE study results are widely generalizable to older patients with diabetes because the great majority of such patients would have met the inclusion criteria for the study. The same cannot be said for any other ACE inhibitor trial.

Increased prescription of ramipril for diabetic patients based on the HOPE results represents not hype, but implementation of high-quality evidence from a large, adequately powered randomized trial.

Ronald J. Sigal
Clinical Epidemiology Program
Ottawa Health Research Institute
Ottawa, Ont.

References

1. Pilote L. Ramipril use in Canada: HOPE or HYPE? [editorial]. *CMAJ* 2003;168(5):568-9.
2. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation (HOPE) Study Investigators. *Lancet* 2000;355:253-9.
3. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med* 2000;342:145-53.

Competing interests: Dr. Sigal has received speaker fees and research support from Aventis, the manufacturer of ramipril.

[Louise Pilote responds:]

My commentary[1] elicited several letters supporting the results of the HOPE study. However, it was not

my intention to belittle the importance of the trial; rather, I wanted to put into perspective the dramatic rise in prescribing rates for ramipril that occurred in Canada around the time the study findings were published.[2]

HOPE was a well-conducted and timely clinical trial, and certainly part of the response in ramipril prescribing rates was appropriate. However, HOPE did not address the use of ramipril immediately after acute myocardial infarction or in patients with congestive heart failure. Yet, as illustrated by Tu and associates,[3] Canadian physicians almost immediately began using ramipril in these subgroups, presumably because of an assumption of a class effect among ACE inhibitors.

Salim Yusuf and Gilles Dagenais quote independent analyses of the cost-effectiveness of ramipril. These latter studies were published months to years after publication of the HOPE trial, but the use of ramipril increased sharply at the time of and even before publication of the trial. Yusuf and Dagenais also suggest that Canadian cardiologists and internists became familiar with ramipril because of their involvement in the study. The fact that prescriptions of ramipril increased even before the trial was published and well before the subgroup and cost-effectiveness analyses appeared suggests that physicians began using ramipril for reasons other than the evidence available at the time.

David Fitchett refers to the AIRE study, which was published in 1993.[4] In that study, ramipril was given "late," more than 48 hours after acute myocardial infarction in patients with evidence of congestive heart failure. In fact, none of the trials that examined the early administration of ACE inhibitors used ramipril. Fitchett suggests that we should assume a class effect for ACE inhibitors, but what is the evidence for this assumption? The recent withdrawal of cerivastatin from the market should serve as a reminder that the drugs within a class may not all have the same benefits and side effects.

Wally Shishkov's concerns about the use of medication to prevent type 2 diabetes mellitus are warranted. Basic lifestyle modifications should be attempted before drug therapy is implemented. Ronald Sigal argues that diabetic patients should be given ramipril on the basis of the HOPE results. I agree, and I do prescribe ramipril for my diabetic patients. The intent of my editorial was to caution physicians against extending the HOPE results to populations not represented by patients in the study.

Finally, if the explanation for the sharp rise in ramipril use is entirely evidence based, why is this remarkable growth in sales almost entirely a Canadian phenomenon? Between 1999 and 2002, the market share of ramipril among ACE inhibitors and angiotensin receptor blockers quadrupled in Canada (from 8% to 31%),(5) while the market share in the United States rose only slightly (from 3% to 6%).[6]

Louise Pilote
Division of Clinical Epidemiology
McGill University
Montréal, Que.

References

1. Pilote L. Ramipril use in Canada: HOPE or HYPE? [editorial]. *CMAJ* 2003;168(5):568-9.
2. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med* 2000;342:145-53.
3. Tu K, Mamdani MM, Jacka RM, Forde NJ, Rothwell DM, Tu JV. The striking effect of the Heart Outcomes Prevention Evaluation (HOPE) on ramipril prescribing in Ontario. *CMAJ* 2003;168(5):553-7.
4. Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. *Lancet* 1993;342:821-8.
5. Canadian CompuScript Audit [database]. Pointe-Claire (QC): IMS Health, Canada; [monthly].
6. US national prescription audit [database]. Plymouth Meeting (PA): IMS [Web site]; [monthly].

Competing interests: None declared.