Patient compliance with drug therapy for diabetic nephropathy

William Clark and colleagues were clearly sensitive to the effects of patient compliance in their study of the cost-effectiveness of angiotensin-converting-enzyme (ACE) inhibitor therapy for diabetic nephropathy.[1] This highlights 3 important assumptions regarding compliance that require further clarification.

First, it was assumed that noncompliers lose renal function at the same rate as patients in the placebo arm of a diabetic nephropathy trial comparing the effects of ACE inhibitors and placebo.[2] It would seem unlikely that patients taking up to 80% of their ACE inhibitor (the definition Clark and colleagues offered for noncompliance) would lose renal function at the same rate as those taking none. The rate at which noncompliers lose renal function should have been subjected to sensitivity analysis.

Second, the authors based their analysis on the results of a patient-interview study[3] in which 34% of patients *stated* cost as the primary barrier to compliance. To suggest that 34% of patients *would* be noncompliant for this reason is a major assumption. A recent observational study of persistence with antihypertensive therapy suggested that the relationship between drug cost and compliance was less clear.[4] The more expensive ACE inhibitors were in fact associated with higher persistence rates. Thus, when one is evaluating the implications of noncompliance, factors other than drug costs must not be ignored.

Finally, provincial drug coverage may not have had as much impact as assumed because a proportion of patients already have the cost of their medications covered through private insurance. Before ACE inhibitor coverage becomes standard practice, we propose that the effect on compliance of providing medications free at the point of delivery should be more thoroughly assessed. If such studies confirm that compliance improves significantly, then consideration could, in fact, be given to developing a national pharmacare program, whereby cost-effective medications, such as ACE inhibitors for diabetic nephropathy, would be provided free to all Canadians.

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Competing interests: None declared.

References

1. Clark WF, Churchill DN, Forwell L, Macdonald G, Foster S. To pay or not to pay? A decision and cost–utility analysis of angiotensin-converting-enzyme inhibitor therapy for diabetic nephropathy. *CMAJ* 2000;162(2):195-8.
2. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD, for the Collaborative Study Group. The effect of angiotensin-enzyme inhibition on diabetic nephropathy. *N Engl J Med* 1993;329:1456-62.
3. Brand FN, Smith RT, Brand PA. Effect of economic barriers to medical care on patients' noncompliance. *Public Health Rep* 1977;92:72-8.
4. Caro JJ, Speckman JL, Salas M, Raggio G, Jackson JD. Effect of initial drug choice on persistence with antihypertensive therapy: the importance of actual practice data. *CMAJ* 1999; 160(1):41-6.

[Two of the authors respond:]

Dyfrig Hughes and Braden Manns suggest that there are 3 important assumptions regarding compliance that require further clarification in our decision and cost–utility analysis.[1]

First, we assumed that noncompliers lose renal function at the same rate as patients in the placebo arm of a diabetic nephropathy trial.[2] We selected 80% adherence as the threshold required for antihypertensive drug effect on the basis of studies[3–6] we referenced in our article.[1] However, some degree of renoprotection may still occur at adherence levels below 80%, as the renoprotective effects of the drug therapy may be independent of the blood pressure effects in this particular disease. Therefore, we do concur that a sensitivity analysis could have been carried out.

Second, Hughes and Manns question whether cost really is the primary barrier for drug adherence for 34% of patients. This assumption is based on a Canadian study that indicated that 34% of the compliance failure was due to cost, representing 17% of patients.[7] We indicated in our article that this was a conservative estimate, as price elasticity has been demonstrated to be as high as 64% in a large randomized controlled study and a very large population study.[8,9] We would contend that the figure we used describing the relationship between drug cost and adherence is conservative. Hughes and Manns also indicate that the relationship was less clear in view of a study by Caro and colleagues that looked at patients in Saskatchewan between 1989 and 1994.[10] They may not be aware that in Saskatchewan during that time period there was a fairly comprehensive pharmacare program, which might explain variations between expensive and inexpensive antihypertensive agents.[11] However, we agree that factors other than drug costs must not be ignored when evaluating the implications of noncompliance.

Finally, we feel that our assumption concerning the proportion of patients already being covered through provincial or private insurance is valid. We concur with Hughes and Manns that the effect on adherence of providing medications free at the point of delivery should be more thoroughly assessed. We also hope that if such studies are undertaken and do show significant improvements in adherence, there would be consideration to developing a national pharmacare program whereby cost-effective medica-

tions such as ACE inhibitors for diabetic nephropathy would be provided free to all Canadians.

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References

1. Clark WF, Churchill DN, Forwell L, Macdonald G, Foster S. To pay or not to pay? A decision and cost–utility analysis of angiotensin-converting-enzyme inhibitor therapy for diabetic nephropathy. *CMAJ* 2000;162(2):195-8.
2. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD, for the Collaborative Study Group. The effect of angiotensin-enzyme inhibition on diabetic nephropathy. *N Engl J Med* 1993;329:1456-62.
3. Sackett DL, Snow JC. The magnitude of compliance and noncompliance. In: Haynes RB, Taylor DW, Sackett DL, editors. *Compliance in health care*. Baltimore: Johns Hopkins University Press; 1979. p. 11-23.
4. Eraker SA, Kirscht JP, Becker MH. Understanding and improving patient compliance. *Ann Intern Med* 1984;100:258-68.
5. Gibaldi M. Failure to comply: a therapeutic dilemma and the bane of clinical trials. *J Clin Pharmacol* 1996;36:674-82.
6. McKenney JM, Munroe WP, Wright JT. Impact of an electronic medication compliance aid on long-term blood pressure control. *J Clin Pharmacol* 1992;32:277-83.
7. Brand FN, Smith RT, Brand PA. Effect of economic barriers to medical care on patients' noncompliance. *Public Health Rep* 1977;92:72-8.
8. Leibowitz A, Manning WG, Newhouse JP. The demand for prescription drugs as a function of cost-sharing. *Soc Sci Med* 1985;21:1063-9.
9. O'Brien B. The effect of patient charges on the utilisation of prescription medicines. *J Health Econ* 1989;8:109-32.
10. Caro JJ, Speckman JL, Salas M, Raggio G, Jackson JD. Effect of initial drug choice on persistence with antihypertensive therapy: the importance of actual practice data. *CMAJ* 1999; 160(1):41-6.
11. Caro JJ, Salas M, Speckman JL, Raggio G, Jackson JD. Persistence with treatment for hypertension in actual practice. *CMAJ* 1999;160(1):31-7.

Access to the morning-after pill in BC

The primary goal of the BC emergency postcoital contraception initiative, which was discussed in a recent *CMAJ* article,[1] is to increase the availability of this important option for women's reproductive health. The resolution of the Society of Obstetricians and Gynaecologists of Canada calling for increased access to emergency postcoital contraception prompted the College of Pharmacists of BC to consider the situation in our province. It was clear that more work was needed to inform women about emergency postcoital contraception and to make it more accessible. Pharmacists can play a vital role in making this happen because of their knowledge of drug therapy and their availability. The threats and violence against physicians who perform abortions serve as a reminder that extreme emotions are associated with issues of reproductive choice and that much more needs to be done to prevent unintended pregnancies.

The *CMAJ* article states that BC will be making Preven a schedule II medication.[1] The hormones for emergency contraception are classed as prescription drugs at the federal level. The provinces cannot change the classification of a drug from prescription to nonprescription by placing it in schedule II. Provincial authorities can, however, explore avenues for permitting pharmacists to dispense a prescription drug without a physician's prescription. One mechanism may be to work in collaboration with a physician. Another option is to create a pharmacists' prescribing schedule. The College of Pharmacists of BC has submitted a resolution to the provincial government calling for the creation of schedule IV. The only drugs in the schedule would be the hormones for emergency contraception. By approving schedule IV, the provincial government would grant pharmacists independent prescribing authority for these products only.

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Reference

1. Sibbald B. Despite some opposition, BC pharmacists to dispense morning-after pill without prescription. *CMAJ* 2000;162(6):876-7.

What exactly are we treating with the morning-after pill?[1] The absence of any medical facts is obvious. The morning-after pill is really an abortion pill. The joining of the sperm and the ovum in the fallopian tubes creates the beginning of a life. All of the DNA that we will require for the rest of our lives is present at that first moment. After that, only the amount of dependency on our parents decreases with time. The morning-after pill prevents the implantation of a unique human individual, tiny but unique and genetically complete.

Is it any wonder that some pharmacists are objecting on ethical grounds? They don't want to see themselves as abortionists. Who can blame them? Let's stick to the facts. Rhetoric about providing a service and reducing violence against physicians obscures the fact that this pill is ending a unique individual's life.

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Reference

1. Sibbald B. Despite some opposition, BC pharmacists to dispense morning-after pill without prescription. *CMAJ* 2000;162(6):876-7.

Managing hypertension in patients with renal disease and diabetes

I congratulate the authors of the 1999 Canadian recommendations for the management of hypertension[1] for their diligent work, but question the recommendations regarding hypertensive patients with diabetic and nondiabetic renal disease. Ample evidence exists to support the use of angiotensin-converting-enzyme (ACE) inhibitors as first-line agents in both of these circumstances, but the selection of dihydropyridine calcium-channel blockers as an alternative therapy for nondiabetic renal disease and the lack of a recommendation for the use of nondihydropyridines in diabetic nephropathy are questionable.

A number of well-designed studies