which only half their patients would undergo this operation).

The third level is uncertainty at the level of the individual partnership between patient and clinician, where unless *both* of them are uncertain which arm of the trial is better for the patient, the patient doesn't join the trial.

I think Francis Rolleston has both nicely described these 3 different levels of uncertainty and correctly pointed out that my original essay was concerned primarily with the third level of uncertainty, that within the individual patient–clinician partnership.[1] Alas, he then proposes retaining the term "clinical equipoise" to denote the first level, community uncertainty. The disutility of his proposal is immediately revealed in the letter from Ian Shrier, who evokes clinical equipoise in addressing the third level of uncertainty.

I thank these 2 correspondents for making my point.

David L. Sackett
Director
Trout Research & Education Centre
at Irish Lake
Markdale, Ont.

Reference

1. Sackett DL. Why randomized controlled trials fail but needn't: 1. Failure to gain "coal-face" commitment and to use the uncertainty principle. *CMAJ* 2000;162(9):1311-4.

The value of industry-sponsored studies of initial antihypertensive therapies

Despite serious concern,[1,2] James Wright continues to dismiss a body of evidence from actual practice that newer classes of antihypertensive drugs may improve adherence to therapy and therefore blood pressure control.[3–5] We believe that it is he who has "misse[d] the point."[6] The issue here is not that observational data should replace data from clinical trials, but simply that results from real-world studies are also worth considering in the initial choice of antihypertensive therapy.

Wright's summary dismissal of this evidence is based on the contention that the results of observational studies are contradictory and that those showing worse compliance with diuretics reflect the vested interest of the sponsoring companies. The clincher, he avows, is that such studies are irremediably biased anyhow whereas blinded randomized trials are not. His first and third points are clearly incorrect. All studies of adherence in patients with newly diagnosed hypertension have produced similar results, demonstrating greater adherence to angiotensin-converting-enzyme inhibitors.[7] The observational studies that have not shown these results[8,9] are about patients with chronic hypertension, that is, patients who already have established prescription therapy; the findings of the latter studies are thus irrelevant in this debate.[10] Although observational studies are clearly more prone to confounding, randomized trials are by no means immune to bias. More importantly, randomized trials severely aggravate the Hawthorne effect, and blinding of patients precludes proper study of the question of the relation of compliance to drug characteristics: the method Wright advocates will *not* answer this question.

Funding by drug manufacturers should always be taken into account when interpreting results, but it does not justify summary dismissal of the findings. Apart from disclosing the funding sources for our study, we reported our methodology in detail: neither our data source (Saskatchewan Health) nor our straightforward methods were in any way influenced by the company that partly funded the study (the company was interested in irbesartan, a drug that was not included in our report).[11]

Wright's own position on these matters would have been more widely communicated if he had addressed the studies of actual practice, not just presented arguments against their validity. We remain convinced that proper assessment of first-line antihypertensive therapy means looking at all available evidence, including the observational studies. Wright's failure to acknowledge these data is a serious and misleading omission and discourages a deeper understanding of the reasons for our poor performance in managing hypertension.

J. Jaime Caro
Caro Research Institute
Montreal, Que.
Krista Payne
Caro Research Institute
Montreal, Que.

References

1. Spence JD. First-line drugs for hypertension [letter]. *CMAJ* 2001;164(2):176-7.
2. Caro JJ, Payne K. Real-world effectiveness of antihypertensive drugs [letter]. *CMAJ* 2000; 162(2):190.
3. Wright JM. Choosing a first-line drug in the management of elevated blood pressure: What is the evidence? 1: Thiazide diuretics. *CMAJ* 2000; 163(1):57-60.
4. Wright JM. Choosing a first-line drug in the management of elevated blood pressure: What is the evidence? 2: β-Blockers. *CMAJ* 2000; 163(2):188-92.
5. Wright JM. Choosing a first-line drug in the management of elevated blood pressure: What is the evidence? 3: Angiotensin-converting-enzyme inhibitors. *CMAJ* 2000;163(3):293-6.
6. Wright JM. First-line drugs for hypertension [letter]. *CMAJ* 2001;164(2):178.
7. Payne KA, Esmonde-White S. Observational studies of antihypertensive medication use and compliance: Is drug choice a factor in treatment adherence? *Curr Hypertens Rep* 2000;2:515-24.
8. Jones JK, Gorkin L, Lian JF, Staffa JA, Fletcher AP. Discontinuation of and changes in treatment after start of new courses of antihypertensive drugs: a study of a United Kingdom population. *BMJ* 1995;311:293-5.
9. Hamilton RA, Briceland LL. Use of prescription-refill records to assess patient compliance. *Am J Hosp Pharm* 1992;49:1691-6.
10. Wright JM, Lee CH, Chambers GK. Real-world effectiveness of antihypertensive drugs [letter]. *CMAJ* 2000;162(2):190-1.
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.

[The author responds:]

I am pleased that Jaime Caro and Krista Payne have kept this discussion alive, thus allowing me to explain my position at greater length.[1,2] The objective of scientific research is to minimize bias as much as possible, which is why the double-blind randomized trial is the gold standard. In a perfect world, observational studies of adherence to dispensed drugs might be valid. However, the real world is far from perfect.

In my opinion, the studies mentioned by Caro and Payne[3,4] are predominantly a measure of the effect of

an intensive drug-advertising program. This type of program is able to bias such studies in at least 3 ways.

The first and most obvious way is the effect of free samples. When these studies were carried out, many patients were being given free samples of angiotensin-converting-enzyme (ACE) inhibitors; patients who did well on the sample received a prescription for the drug, and patients who did poorly were tried on something else. In contrast, patients whose initial therapy was thiazides (no free samples) were all given a prescription from the start. Because free samples are not measured as dispensed drugs, the appearance created is that adherence is better for ACE inhibitors than for thiazides.

The second way is the strong physician bias that intensive advertising creates in favour of ACE inhibitors and against thiazides. This bias is conveyed to the patient and affects adherence to treatment.

The third way is that a drug company limits its funding to studies of those populations for which it is relatively certain what the outcome will be, on the basis of its own data. This is called selection bias. Caro and Payne imply that the company funding their study[3] was not biased. They neglect to mention that Bristol–Myers Squibb markets fosinopril, an ACE inhibitor.

I reiterate that the best way to measure adherence to different antihypertensive therapies is to use the randomized double-blind design. In this type of study, adherence is affected by the drug's characteristics and not by other influences.

James M. Wright
Departments of Pharmacology
& Therapeutics and Medicine
University of British Columbia
Vancouver, BC

References

1. Wright JM. First-line drugs for hypertension [letter]. *CMAJ* 2001;164(2):178.
2. Wright JM, Lee CH, Chambers GK. Real-world effectiveness of antihypertensive drugs [letter]. *CMAJ* 2000;162(2):190-1.
3. Caro JJ, Salas M, Speckman JL, Raggio G, Jackson JD. Persistence with treatment for hypertension in actual practice. *CMAJ* 1999;160(1):31-7.
4. Payne KA, Esmonde-White S. Observational studies of antihypertensive medication use and compliance: Is drug choice a factor in treatment adherence? *Curr Hypertens Rep* 2000;2:515-24.

Lithotripsy comes to Ottawa ... at last

In July 2000 the Ontario Ministry of Health and Long-Term Care announced that it would fully fund a lithotripsy program in Ottawa. I write to alert readers to the complexity of getting things done with this ministry and to thank the many people who helped to finally bring lithotripsy therapy to Eastern Ontario.

Extracorporeal shock-wave lithotripsy for the management of ureteric calculi became available in the early 1980s; 2 machines were in operation in Ontario by 1989, in Toronto and London.

Until recently, lithotripsy was not available in Ontario east of Toronto. Patients in the Ottawa region were required to travel at their own expense to Toronto, London or Montreal for treatment. The waiting time for urgent therapy in Montreal was 2 weeks.

In 1996 my colleagues and I applied to the Ontario Ministry of Health and Long-Term Care to make extracorporeal shock-wave lithotripsy available in Ottawa. At that time Ottawa was the largest city in North America without a lithotripsy machine. The ministry refused our request, citing the capital investment to purchase the machine, the ongoing maintenance costs and the fact that Toronto and London could handle the patient load.

Because the ministry's refusal was based primarily on cost, we responded by carefully monitoring the cost of treating Ottawa-area patients with more invasive procedures at the Ottawa Hospital – General Campus. We showed that by offering lithotripsy to just 250 patients per year (of an estimated 700 eligible patients per year from this region) we would in fact save money.

Our greatest concern was that patients in Ottawa were being treated more invasively than other patients in