Raloxifene remains an option

My family practice has many geriatric patients. Raloxifene is one of several drugs I routinely prescribe for these older people. I am writing in response to your Critical Appraisal article[1] in the October 2001 issue regarding raloxifene, and specifically the Multiple Outcomes of Raloxifene Evaluation (MORE) trial.[2]

This large study involves 7705 women in 25 countries. It is a placebo-controlled, blinded, randomized trial. Conclusions drawn from well constructed trials of this type are considered to have the highest level of evidence in evidence-based medicine.[3] The quality of evidence provided by the MORE trial is level I.

The authors of your Critical Appraisal article comment that this trial "based its findings on examination of radiographs rather than people." This is not entirely the case, as the trial did specifically look at those women with clinical vertebral fractures. These were women who presented with back pain, suggesting fractures. This is very relevant to modern clinical medicine. This subgroup of women had a fracture risk reduction with raloxifene similar to the other women taking raloxifene in the study.

The authors also comment that conclusions about the positive effects of raloxifene on women's spines cannot be made, given the fact that these women were also receiving calcium and cholecalciferol, both shown to reduce fractures in older people with osteoporosis. Both the raloxifene and the control groups, however, took calcium and cholecalciferol at the same dose, hence allowing one to conclude that the positive effect on women's spines would be from the raloxifene. Furthermore, the doses of calcium and cholecalciferol used were below current recommended doses and might not have had any effect in either group.[4]

Further analysis of the MORE trial demonstrated that the number of women withdrawing from the study due to adverse events was about the same in the raloxifene groups as in the placebo group. There was no statistically significant difference. My clinical experience has shown raloxifene to be very well tolerated.

For me, a careful analysis of the MORE trial has yielded somewhat different conclusions from those put forward by your authors. After appropriate discussion of the risks and benefits of therapy, I will continue to prescribe raloxifene to my patients, and it should remain an important option for osteoporosis patients for years to come.

—Douglas W. MacIver, MD, CCFP
St Albert, Alta
by fax

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Response

I thank Dr MacIver for his letter and his prompting of a more complete discussion of the value of raloxifene. He makes some excellent points. I will discuss them one at a time.

1. Dr MacIver was concerned about the statement that the MORE trial "based its findings on examination of radiographs rather than people." The authors identified that the primary outcome measure was new, confirmed vertebral fractures. Vertebral radiographs were obtained at baseline, 24 months, and 36 months. Dr MacIver is right in that when symptoms of vertebral fracture were reported in a small number of subjects at 6-month interim visits, additional radiographs were taken. I believe our point was actually more about

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the fact that vertebral fractures are a surrogate outcome, where a radiologist measures the x-ray with a ruler, and patients are usually asymptomatic. In the Critical Appraisal series we try to focus on outcomes that are most important to patients and family doctors, because this allows us to wade through the medical literature and prioritize the most effective therapies. In this case it is hip fracture rates that were not statistically different from the placebo group despite the large number of women in this trial. I still stand by the sentence, as I do believe this trial's outcomes were predominantly based on radiographic findings that largely did not affect the quality of patients' lives.

2. Concern was raised about the effectiveness of raloxifene and the effect of calcium and cholecalciferol because doses, particularly for cholecalciferol, were less than those used in other trials to prevent fractures. Dr MacIver assumes that prevention was, therefore, due to raloxifene. This might be true, but it might also mean that the true benefit of raloxifene over calcium and cholecaciferol is less than what is reported in this trial.
3. Dr MacIver states that "Further analysis of the MORE trial demonstrated that the number of women withdrawing from the study due to adverse events was about the same in the raloxifene groups as in the placebo group." I am not sure whether he is referring to another analysis of this trial, but in the main outcomes the authors state that "[W]omen in the raloxifene groups withdrew from the study more often because of adverse events and developed more thrombosis (1% vs 0.3%)." I do agree with Dr MacIver that this medication can be well tolerated, but I find the thrombosis rate quite worrisome given the seriousness of the condition.
4. Dr MacIver concludes by stating, "After appropriate discussion of the risks and benefits of therapy, I will continue to prescribe raloxifene to my patients, and it should remain an important option for osteoporosis patients for years to come." I agree with this. I am particularly interested in following the story of breast cancer prevention. At this point, my own position is that alendronate has the best evidence (ie, hip fracture prevention data), etidronate is the most practical (inexpensive, easy to take with good supporting cohort data), and hormone replacement therapy is most helpful for the symptoms of menopause. I look forward to further data on selective estrogen receptor modulators and possibly changing my position.

—Michael Evans, MD, CCFP

(Co-author Dr Hathirat is in Thailand and could not be reached for comment.)

Aboriginal health and family physicians

I read Dr Smylie's reference in her December 2001 article,[1] "Building dialogue," quoting me from a newspaper article about the problems in Sheshatshiu, Lab: "This is a spiritual issue and no amount of money can heal the spirit." This is followed by her declaration that "As an Aboriginal person, I have been taught that I can speak only for myself. To speak for others, especially members of a community of which I am not a part, would be to show disrespect."

I ponder these words, look at their context, and feel their bite. Yet, I agree with her. To speak for another person is disrespectful. Further, this has not only to do with being aboriginal, it has to do with being a decent and respectful human being. It is also especially true when the person whose voice is usurped is perfectly capable of speaking for himself or herself. I can understand the frustration that perhaps Dr Smylie and all aboriginal people feel when you perceive that, as Peter Penashue, President of the Innu Nation said, "Another outsider is telling you what to do." Certainly, the silencing of aboriginal voices since white people arrived in North America has left a devastating legacy.

At this moment in history, however, there is a heartbreaking catch. What about the children, neglected and abandoned by parents gone to bingo, perhaps even with money distributed by the election campaigns of the band council? What about the babies turned to cinders in burning homes while their parents are drunk on the day that the Child Tax Credits arrive in the mail? What about the babies born with fetal alcohol syndrome? Those little children all have names and lovely faces. In one small community, I know them. I know all the ones who died. I held them when they were born and said a quiet prayer in the hope that healing would come soon to their circumstances.

The challenge, then, for me has been this: when is it disrespectful to speak about a community to which I do not belong, and when is it impossible to stay silent? When is my silence simply an extension of the silence of all of those little, dead children? We each have our own breaking point in this dilemma. I can only listen to, and hold the intentions of love and compassion in, my own heart.

Dr Smylie is a Métis woman and a family physician. I am very interested in finding out how she has responded to these impossible circumstances in her own practice. Of course, I will go to the websites suggested in her article. At the same time, I would be very interested in "building dialogue" with her concerning these issues. I know there are many other caregivers who have practised medicine in cross-cultural settings. Some have been similarly dismissed when very real issues of corruption and neglect have been brought to the table. It is true, no doubt, that some of these caregivers