The paper by Dr Khan describes in Table 4 five "well conducted studies," four of which provide "level I" evidence and one "level II" evidence comparing the use of bisphosphonates with a placebo. The outcome measure is reduction in relative risk of fracture. For three of the five studies, the reduction of relative risk for hip fracture was not significant. The relative risk reduction for new vertebral fractures ranged from 18% to 47% in the four studies where this was an outcome measure.

As a treating physician, reduction in relative risk does not tell me very much. It would have been much more useful to know the difference in prevalence of fractures between treated and placebo groups. The number of patients needed to treat to prevent one fracture also would have been helpful.

The second reference[4] in Dr McKercher's editorial suggests 90% of women older than 65 should be candidates for bone mineral density testing. The predictive value of bone mineral density in terms of relative risk of fracture varies with age and has little value in younger age groups. For example, as quoted in the guidelines, a 25-year-old with a low bone mineral density (T score of –2.5) has a very low risk of fracture, as low as that of a 25-year-old with a high bone mineral density. Similarly, a 55-year-old with a low bone mineral density is at 10 times less risk than a 75-year-old with the same low bone mineral density of having a fragility fracture of the hip or vertebra.

A recent editorial[5] in the *British Medical Journal* concluded,

> Against a background of controversy over disease definition, poor predicted value of bone density measurement, and heavily advertised expensive therapies offering marginal benefit to postmenopausal women, corporate-backed promotional activities are attempting to persuade millions of healthy women worldwide that they are sick.

In contrast, on the front cover of April's *Canadian Family Physician* were the words "Osteoporosis. Silent Epidemic." Who is correct?

Readers of *Canadian Family Physician* would have been better served if a health epidemiologist not associated with the osteoporosis industry had the opportunity to provide a critical analysis of the efficacy of screening and treatment. In an era of increasing demands for health resources and finite funding, we need to be better convinced that the recommended screening and treatment for this condition is appropriate.

—John Sehmer, MD, MSC, CCFP
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by e-mail

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Show us the numbers

Thank you for the article[1] on osteoporosis. It does have some helpful information. However, there could be a few improvements, especially if this information is supposed to educate us. We should not forget to indicate *absolute risk reduction* in addition to relative risk reduction. As you can imagine, relative risk reduction can be extremely misleading. For example, if the incidence of a disease after a treatment drops from 2 per 1000 to 1 per 1000 that is a whopping 50% relative risk reduction! That sounds great, but the absolute risk reduction is 0.1%, meaning the treatment is pretty useless. We need to know what these numbers are, particularly if we might change our practice patterns.

It is a great drug company trick to publish only relative risk reductions. I believe that some journals are refusing to publish articles unless the absolute risk reduction numbers are included. We should do the same. We should also include the number needed to treat (NNT) and the number needed to harm (NNH). It is impossible for me to judge the use of a drug without these numbers.

I would also like to point out that the finding of risedronate causing a 30% relative reduction in the risk of hip fracture should be brought into question because it was found through subgroup analysis, as the author points out. I think it is dangerous to make positive judgments on subgroup analyses, and I believe that your editors should be making this very clear to readers. These results can form only the basis for a new experiment. They are, otherwise, data dredging.

Finally, whenever there are studies done wherein the tested drug is tried at several different doses, I would suggest high suspicion in interpreting these results. I refer to the calcitonin tests. I think the author does hint at this problem. We should be a little more up front in explaining why these types of experiments are pets of the drug industry because the more doses tested, the greater the chance, simply by chance alone, that one of them will be shown to be "beneficial." These results cannot be trusted.

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Response

I agree with Dr Larocque that there are limitations in using relative risk alone, and absolute risk is important to consider. Relative risk reduction of greater than 25% is generally considered to be clinically significant. I refer Dr Larocque to an excellent book.[1] The authors describe why relative

risk reduction is important in evaluating drug therapy and assessing clinical usefulness for intervention. The relative risk reduction is a necessary measure of clinical significance. Absolute risk reduction has shortcomings with respect to clinical usefulness. The reciprocal of absolute risk reduction is the number of patients needed to treat in order to prevent one complication of the disease. This is useful, as it emphasizes the effort needed in order to accomplish a treatment target. It also enables us to estimate the cost of treatment. There is, however, an important consideration when evaluating the number needed to treat. This number can vary drastically depending upon the study population and therefore should *not* be used for comparison between drugs in the absence of a head-to-head trial.

My article quoted a 30% reduction in the relative risk of hip fracture with risedronate. Dr Larocque states that the relative risk reduction of 30% was obtained by subgroup analysis. This is not the case. The 30% reduction was obtained from the overall data. The subgroup analyses identified a 40% reduction in women with osteoporosis as described in the article. A 60% reduction was seen in those women who also had pre-existing vertebral fractures at baseline.

In the PROOF trial evaluating calcitonin therapy,[2] a dose response was not seen. The reasons for this are not clear and could have been related to the drop-out rate. Clearly, what was statistically significant was a reduction in vertebral fracture with the 200-IU dose, on which basis calcitonin was approved by both the Food and Drug Administration and the Health Protection Branch for treatment of osteoporosis.

We must remember that results from clinical research are very carefully considered by both the Food and Drug Administration and the Health Protection Branch, and the possibility of "chance" alone contributing to the data is excluded by detailed statistical analysis in well-designed clinical trials with fracture as a primary outcome.

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Is expensive medicine worth it?

Having myself done a review of the literature on the same subject, I read with interest the article[1] by Dr Papsin and Ms McTavish, "Saline nasal irrigation," in the February issue of *Canadian Family Physician*.

I had undertaken this research because residents were prescribing "Hydrasense" for acute rhinosinusitis to patients at our walk-in clinic. Because we were working in a disadvantaged area, I wondered whether studies supported such an expense for these patients.

As the authors mentioned in their "Quality of evidence" section at the beginning of the article, most studies on this subject are small and not placebo-controlled. The best study I found was the one by Adam et al[2] cited as reference 14 by the authors. It showed no difference in outcome whether patients were treated with a hypertonic nasal solution, an isotonic nasal solution, or observation for acute rhinosinusitis. I concluded there was no evidence base for asking patients to buy such an expensive product.[3]

Papsin and McTavish's objective was to review the literature for clinical trials of the efficacy of saline nasal irrigation. The authors did not mention, as is usual in this type of research, what criteria they used to include or reject articles. It seems that they retained all the articles they found. I cannot understand why certain articles (cited as references 8, 22, 23, and 25), which they describe in the text, are not included in Table 1, "Clinical studies of saline irrigation."[1]

I found the section on rhinosinusitis weak both in its literature review and in its content. I was shocked that the authors ended this section by describing without comment the study by Seppey and Krayenbuhl (reference 22).[4] The authors reported the conclusions without analyzing or criticizing them. I tried to obtain the article by Seppey and Krayenbuhl, but it was published in a journal not listed on MEDLINE. The authors' summary suggests the study was not randomized and not placebo-controlled and did not mention the inclusion criteria or which antibiotic was used. The authors suggest that most patients got better with only 5 days of antibiotic therapy, rather than the usually recommended 10-day treatment, because nasal irrigation was given with 5 days of antibiotics: "Frequent nasal lavage can reduce the length of antibiotic therapy." What we must understand when we do a literature review on the subject of acute rhinosinusitis is that, in most studies of antibiotics versus placebo, most patients get better while receiving placebo and that there is often no difference in rates of improvement—it is not surprising, then, that the patients in this study got better with only 5 days of antibiotics.[5-11]

If we want to reduce antibiotic resistance, we should simply refrain in general from prescribing antibiotics during the first few days of acute rhinosinusitis (unless it is a question of severe sinusitis, which was excluded by the antibiotic-placebo studies). The role of nasal irrigation remains to be defined.

The section on allergic rhinitis would have been interesting, but there again the authors only described and did not analyze the two studies of Georgitis.[12,13] The authors used the first of these studies to affirm: "Nasal irrigation has been recommended as an adjunct therapy to flush out mucus and irritants and improve the flow of