CMAJ's 100th anniversary

I was delighted to see in the Jan. 11 issue of *CMAJ* not only a dedicated cover but also several pertinent articles celebrating the 100th anniversary of *CMAJ*.[1–3] The cover photo of Sir William Osler is incredible. I wonder how many of the students in that amphitheatre can be identified?

Special thanks are owed to Cindy L. Stelmackowich, who discovered and submitted the cover photo of Osler teaching students at a clinic at the Royal Victoria Hospital in Montréal in 1906.

To date, although we have seen a number of incredibly outstanding Canadian researchers and physicians, no one has really replaced Sir William on an international basis. What a legacy!

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References

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2. Turnbull J. 100 years and counting. *CMAJ* 2011; 183:16.
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***CMAJ* 2011. DOI:10.1503/cmaj.111-2024**

Osteoporosis guidelines miss big picture

Infants, all with low bone density, don't break bones. The bones bend, because the structural component is mainly collagen I and III, "ropes" along which bone mineral builds and rebuilds after osteoclasts remove bone with microcracks. The authors of the recently published guidelines suggest that they no longer focus on treating bone mineral density, but that is exactly what they do, as per their specified pharmacologic-based search-and-exclusion criteria.[1]

Apart from welcome references to the calcium management prohormone vitamin D_3 (up to 2000 IU/d requires no monitoring), the emphasis is on bisphonates, a class of drug that "disables" osteoclasts, thereby mimicking their terrible role in osteopetrosis.[2]

Obviously, bone density affects spinal compression fractures (that are 80% asymptomatic); however, simply increasing density may make bones more brittle unless the toughness factor, collagen, is simultaneously improved. The absence of annual "numbers needed to treat" in the guidelines for spine and particularly hip fractures from bisphosphonates is especially disturbing.

Largely excluded from the search criteria are the word collagen and any of the vitamins and minerals that affect and control collagen synthesis and quality (vitamin C, the homocysteine-lowering B vitamins B_2, B_6, B_9 [folate], B_{12}, copper and iron).[1] Several of these vitamins (and homocysteine levels that are needlessly high because of low vitamin intake) are risk factors for fracture. For example, a placebo-controlled homocysteine-lowering study using only two B vitamins found an 80% reduction in hip fractures in two years, likely as a result of improved collagen quality since bone density and falls were identical.[3]

The guidelines need to be expanded: the focus on just bone density misses an important part of the picture.

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3. Sato Y, Honda Y, Iwamoto J, et al. Effect of folate and mecobalamin on hip fractures in patients with stroke. A randomized controlled trial. *JAMA* 2005; 293:1082-8.

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Papaioannou and colleagues stated that bisphosphonates reduced "the risk of vertebral fracture by 30% to 70%, depending on the agent and level of adherence."[1] This statement does not provide enough information for one to make informed decisions about oral bisphosphonate use.

First, the statement only recognizes fractures in the vertebra, not other sites, including nonvertebra and the hip. Some oral bisphosphonates provide benefits to some sites but not others. The updated 2010 Cochrane reviews of oral bisphosphonates provide information about site-specific fracture prevention.[2–4] The guidelines do not present data from these reviews.

Second, the recommendations to use bisphosphonates to prevent fractures do not differentiate between primary and secondary prevention. According to the Cochrane reviews, neither etidronate nor risedronate has shown benefits in primary prevention.[3,4] Alendronate is the only oral bisphosphonate that seems to have some benefit in primary prevention with respect to vertebral fractures.[2] However, the reduction was found for only radiographic vertebral but not clinical vertebral fractures.[5] Therefore, the clinical importance of this result is debatable.

Finally, the magnitude of fracture reduction is presented in relative terms instead of absolute risk reductions. Oral bisphosphonates do not lead to a reduction in clinical fractures for primary prevention.[2–4] For secondary prevention, oral bisphosphonates reduce the risk of hip fracture by about 1%,[2,4] nonvertebral fracture by about 2%[2,4] and vertebral fracture by about 6%.[2–4] The recommendations for pharmacologic therapy should include this information.

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Intention-to-treat and per-protocol analysis

I congratulate *CMAJ* and Boutis and colleagues for a brilliant research paper.[1] Intention-to-treat analysis is a comparison of the treatment groups that includes all patients as originally allocated after randomization. This is the recommended method in superiority trials to avoid any bias. For missing observations, "last value carried forward" is the recommended method.

Per-protocol analysis is a comparison of treatment groups that includes only those patients who completed the treatment originally allocated. If done alone, this analysis leads to bias.

In noninferiority trials, both intention to treat and per-protocol analysis are recommended; both approaches should support noninferiority. In the article by Boutin and colleagues, intention to treat should have included 50 patients in either group as per randomization or at least 45 in the group with splints (in 4 patients, the diagnosis was wrong) and 50 in the group with casts; this may change the results to indicate a borderline effect. In that article, the analysis was done with 43 patients in the splint group and 49 in the cast group, which appears to be a per-protocol analysis, though it was called an intention-to-treat analysis. Hence, noninferiority can be concluded only after analysis by both approaches.

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1. Boutis K, Willan A, Babyn P, et al. Cast versus splint in children with minimally angulated fractures of the distal radius: a randomized controlled trial. *CMAJ* 2010;182:1507-12.

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We thank Dr. Shah for his thoughtful comments on our article.[1] As he pointed out, 50 patients were initially randomized to each treatment arm. The four patients randomized to the splint group for whom there were diagnostic errors had to be excluded immediately for safety reasons because the fractures required a different treatment strategy. Some experts would advocate continuation of such patients in the trial, while others would agree that patients enrolled in error should be excluded. We adopted the latter approach because all errors in enrolment were related to diagnostic mistakes that were revealed within 24 hours after randomization.

Among the remaining 46 patients in the splint group and 50 in the cast group, we did not have any primary outcome data for 4 (3 splint, 1 cast) because they were lost to follow up for this outcome. We chose not to account for missing data beause it was such a small number of patients and unlikely to affect the outcome. However, Dr. Shah raises a valid point. We conducted the analysis again, giving the missing cast patient the highest possible score of 100 and the three missing splint patients the lowest observed score in their group (73.28). The lower limit of 90% confidence interval was then –3.37 and the p value < 0.0001, thereby rejecting the null hypothesis that the splint is worse than the cast by more than 7 points. These results support the original findings in our article.

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Electronic medical records: small can be idiosyncratic

In the article referring to Canada Health Infoway needing a watchdog,[1] a few things should be considered. Thirty years ago, I was involved with a grassroots approach to try to build an electronic medical record (EMR). It soon became clear that to develop a high-performance product was going to take a multimillion-dollar effort. I have since seen one attempt after another to do the same thing; typically the products are incomplete, use impoverished information models and have idiosyncratic functionality. The problem is that physicians keep buying these products.

In one instance, my office accumulated about 800 000 lab results over a 10-year period. When we changed to a different EMR vendor, the identifier for each test was wiped out because the provincial requirement did not include that identifier. The problem was that the needs of the end user were not being met by the laboratories using legacy systems, and that those who set the provincial requirements did not not recognize this as an issue.

The requirements for a high-performance EMR are not immediately apparent to typical clinical users. They don't seem to be apparent to some EMR vendors who listen to those typical users. There seems to be a widespread awareness of the tremendous amount of work that has been done to determine EMR requirements. If this work was actually considered, we could have made an impressive leap forward in EMR functionality. However, there are so few people interested that there is no critical mass to perform the work on a small scale; a national effort is required.

Although there could be improvements at Infoway, I think the larger problem is that owners and funders of outdated legacy systems are not willing to move forward with systems that would be more conducive to delivering what is needed today.

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Some letters have been abbreviated for print. See www.cmaj.ca for full versions.