Impact of adverse news media on prescriptions for osteoporosis: effect on fractures and mortality

Paul J Sambrook, B E Christopher Nordin and Alastair N Goss

To the Editor: The article by Philip Sambrook et al on the impact of adverse news media on prescriptions for osteoporosis[1] contains a number of serious errors and ignores more recent data.

Their article quotes the estimated incidence of osteonecrosis of the jaw (ONJ) after oral bisphosphonate treatment for osteoporosis to be between 1 in 10 000 and 1 in 100 000 patient treatment-years. This is in fact a gross underestimate.[2] The results of an independent study funded and conducted by the United States Food and Drug Administration (FDA) found an incidence of between 1 in 537 and 1 in 1537.[3] This result is similar to that of an independent Australian study, which found an incidence of 1 in 296 to 1 in 1130.[4] Thus, there is evidence that bisphosphonate-associated ONJ is much more common in patients treated with oral bisphosphonates for osteoporosis than the authors claim.

Bisphosphonate-associated ONJ is also much more serious than presented. Patients with ONJ can be affected for years. The condition causes considerable morbidity, with greater interference in a patient's life than the condition of osteoporosis and vertebral fractures.

It should be noted that the FDA study[3] and the Australian study[4] were based on documented cases of ONJ, whereas the study by Sambrook et al[1] was not based on actual fractures. It is unfortunate that, despite the wording of the Pharmaceutical Benefits Scheme (PBS) regulations, the Pharmaceutical Benefits Advisory Committee has let it be known that osteoporosis diagnosed by bone mineral density is not a requirement for PBS-supported bisphosphonate therapy — all that is required is a minimal trauma fracture, although it is well known that most patients with minimal trauma fracture do not have osteoporosis (however that is defined).[5]

The issue of adverse effects of bisphosphonate treatment for osteoporosis is currently being tested by a US class action. In the bellwether case of *Boles v Merck & Co*,[6] the issue being tested is whether it was appropriate to prescribe alendronate for a patient with osteopenia but no fractures, and how much this treatment contributed to the patient's end-stage ONJ. The plaintiff had exposed bone, constant pain, a pathological fracture, and pus dripping from her chin. The New York Supreme Court found in her favour.

Despite the claim by Sambrook and colleagues that unbalanced media coverage "has the potential to do more harm than good",[1] the media do have an important role to play in exposing to the public the risks of pharmaceutical products and the actions of some pharmaceutical companies. It should be noted that Professor Sambrook was not only involved in *The 7:30 Report* current affairs program, but was also subsequently granted the unusual right of reply on that program. Following these two programs, the public made its decision based on facts about the incidence and morbidity of ONJ that have been confirmed by recent independent studies.[3,4,6]

Competing interests: Alastair Goss has been a consultant to Merck and Novartis on ONJ, and has provided expert testimony for the plaintiffs in the US class action against Merck with respect to alendronate.

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4 Mavrokkoki T, Cheng A, Stein B, Goss A. Nature and frequency of bisphosphonate-associated osteonecrosis of the jaws in Australia. *J Oral Maxillofac Surg* 2007; 65: 415-423.
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6 *Boles v Merck & Co.* Case no. 06-CV-9455. In re Fosamax products liability litigation, MDL 1789, US District Court, Southern District of New York (Manhattan). ❑

Philip N Sambrook, Jiang S Chen, Judy M Simpson and Lyn M March

In reply: Readers will probably deduce that Paul J Sambrook is no relation of Philip N Sambrook.

The Australian Broadcasting Corporation, which aired *The 7:30 Report* that Paul Sambrook and colleagues refer to, subsequently acknowledged in writing that there were a number of factual errors in the original program. Under these circumstances, a right of reply was entirely appropriate.

There is ongoing debate about the incidence of osteonecrosis of the jaw (ONJ), but as the modelling used in our study[1] did not involve any assumptions about this, it is irrelevant to our findings. The studies by Lo et al[2] and Mavrokkoki et al[3] did not report *incidence* of ONJ — they reported prevalence. Moreover, one of the coauthors of the letter by Paul Sambrook et al (above) has published that the estimates by Mavrokkoki et al, being from a retrospective postal survey, must be viewed with caution.[4] The Lo et al study was approved by an institutional review board of the United States Food and Drug Administration (FDA), not "funded and conducted" by the FDA, as Sambrook and colleagues state in their letter.

There have been numerous studies of the effects of vertebral fractures and osteoporosis on quality of life. The authors claim that ONJ causes greater interference to a patient's life than osteoporosis or vertebral fractures, but cite no references to justify this bald assertion.

The US court case of *Boles v Merck & Co*[5] was not an "independent study" (as implied in the last paragraph of the letter by Sambrook et al), but a legal proceeding that is being appealed. One of the coauthors of the letter was a paid expert for the plaintiff.

ONJ is a serious complication of bisphosphonate therapy in the small proportion of affected individuals. We agree that patients need to be informed of the risks of therapy, but they also need to be informed of the consequences of not taking therapy (ie, the benefits forgone) to make a really informed decision. Our article was intended to let patients understand what those consequences might be.

The courts are certainly not the place for informed debate. And the media should appreciate that unbalanced reporting can have significant consequences.

Competing interests: Philip Sambrook serves on the medical advisory boards of and has received speaker fees from Amgen, Merck Sharp & Dohme, Novartis, Sanofi-Aventis and Servier.

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1 Sambrook PN, Chen JS, Simpson JM, March LM. Impact of adverse news media on prescriptions for osteoporosis: effect on fractures and mortality. *Med J Aust* 2010; 193: 154-156.
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