

their actions will result in a net improvement in human health. Until they have done so, the message to trigger happy legislators should be: "Don't just do something. Stand there."

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- 1 Eysenbach G, Dieppen TL. Towards quality management of medical information on the internet: evaluation, labelling, and filtering of information. *BMJ* 1998;317:1496-502.
- 2 Gray JAM. Hallmarks for quality of information. *BMJ* 1998;317:1500.

- 3 Jadad AR, Gagliardi A. Rating health information on the internet. *JAMA* 1998;279:611-4.
- 4 Factors affecting the quality of an information source. <http://biome.ac.uk/guidelines/eval/factors.html> (accessed 2 Oct 2000).
- 5 HON code on conduct (HONCode) for medical and health web sites. www.hon.ch/HONcode/ (accessed 2 Oct 2000).
- 6 Guidelines for AMA web sites. *JAMA* 2000; 283:1602-6.
- 7 Rippen H, Risk A for the e-Health Ethics Initiative. E-Health code of ethics. *J Med Internet Res* 2000;2(2):e9. www.jmir.org/2000/2/e9 (accessed 2 Oct 2000).
- 8 Charatan F. DrKoop.com criticised for mixing information. *BMJ* 1999;319:727.
- 9 Terry NP. Rating the "raters": legal exposure of trustmark authorities in the context of consumer health informatics. *J Med Internet Res* 2000;2(3):e18. www.jmir.org/2000/3/e18 (accessed 2 Oct 2000).

Fluoridation, fractures, and teeth

Fluoride does not cause fractures but its benefits may vary

The benefits to teeth of fluoridating community water supplies are widely acknowledged.¹ A comprehensive summary of the most recent evidence is included in the systematic review by McDonagh et al in this issue of the journal (p 855)² but some concerns persist about possible adverse effects on bone.³ The paper by Phipps et al in this issue of the *BMJ* (p 860) introduces new evidence on the safety of fluoridating community water supplies.⁴ In their multi-centre prospective study, Phipps et al found that ambulatory women aged 65 years or older who had been continuously exposed to fluoridated water for the past 20 years had higher bone mineral density at the lumbar spine and hip and a slightly lower risk of hip and vertebral fractures than women who had not been exposed to fluoridated water. The potential confounding effect of other factors known to be associated with fractures, such as oestrogen use, smoking, and body weight, was controlled for at the level of the individual woman.

This was not the case in earlier ecological studies (cited by Phipps et al) in which higher rates of fractures were found among communities that had fluoridated drinking water when compared with communities without fluoridation. However, a study among residents of the English county of Cleveland who were aged 50 or older and who had had lifelong exposure to naturally high concentrations of fluoride in their drinking water showed no increase in their risk of hip fracture when compared with community controls who used water with naturally low concentrations of fluoride.⁵ In this study potential confounders were also controlled for at the level of the individual woman. Thus there seems to be reasonably strong evidence that an optimal amount of fluoride in drinking water—either added or occurring naturally—does not increase the risk of osteoporotic fractures in elderly people. No evidence of an elevated risk of fractures attributable to using the optimal level of fluoride in drinking water was found in the systematic review by McDonagh et al.²

The association between the fluoridation of community water supplies and the rate of fractures is part of a wider question about the potential of using fluoride for controlling osteoporosis, which is a major public health problem that causes much pain and disability and has considerable costs for society.⁶ The

prevalence of osteoporosis is increasing as the population ages. Bone mineral density and the frequency of fractures are used to assess the exposure of a population to the risk of osteoporosis. Fluoride seems to be the only drug capable of increasing osteoblastic activity and thus bone mineral density. The true value of the gain in bone mineral density remains questionable, however, since its increase after the use of fluoride has been accompanied by both a higher rate of fractures and a lower rate.^{7 8} One theory about the conflicting results is that high doses of fluoride may be harmful and low doses beneficial.⁹ It has also been proposed that adjuvant calcium is necessary for fluoride to be effective.⁹ Finally, the conflicting results may be caused by biases in the studies. Currently, these issues are under thorough scrutiny, and a systematic review is to be published in the near future.⁶

The finding that long term exposure to fluoridated water does not increase the risk of osteoporotic fractures among elderly people should alleviate remaining concerns about the safety of fluoridation.

In terms of benefits, the only aim of community water fluoridation is to prevent dental caries. A recent review of the effectiveness of water fluoridation in the United States shows that previous reductions in mean caries scores of one half to two thirds are no longer attainable because other methods of providing fluoride and the availability of products containing fluoride have reduced the prevalence of caries, thus diluting this measurement of effectiveness.¹⁰ Similar findings have been reported from the United Kingdom.¹¹ The reduction in the relative effect of fluoridation, which is also seen in the systematic review by McDonagh et al has generally not been big enough to call into question the justification for fluoridating water.²

However, a much larger reduction occurred between 1973 and 1982 among 13-15 year olds in Finland: in 1973 the score of decayed and filled teeth was 43% lower in a fluoridated area than in a low fluoride area, whereas in 1982 there was no difference.¹² In Finland preventive dental care is provided free to all children, and this reduction shows that the relative effect of fluoridation can vary strongly depending on different circumstances. Over 360 million people in about 60 countries worldwide are exposed to fluoridated water: more than 10 000 communities and 145 million

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people are exposed in the United States alone.¹³ Given the huge numbers and the fact that the idea of fluoridating community water divides public opinion, the benefits and potential risks of fluoridation require careful and continuous monitoring.

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- 1 Public health service report on fluoride benefits and risks. *MMWR Morb Mortal Wkly Rep* 1991;40:1-8.
- 2 McDonagh MS, Whiting PF, Wilson PM, Sutton AJ, Chestnutt I, Cooper J, et al. Systematic review of water fluoridation. *BMJ* 2000;321:855-9.
- 3 Gordon SL, Corbin SB. Summary of workshop on drinking water fluoride influence on hip fracture and bone health. *Osteoporos Int* 1992;2:109-17.
- 4 Phipps KR, Orwoll ES, Mason JD, Cauley JA. Community water fluoridation, bone mineral density, and fractures: a prospective study of effects in older women. *BMJ* 2000;321:860-4.
- 5 Hillier S, Cooper C, Kellingray S, Russell G, Hughes H, Coggon D. Fluoride in drinking water and risk of hip fracture in the UK: a case-control study. *Lancet* 2000;355:265-9.
- 6 Haguenaer D, Mirmiran S, Welch V, Adachi JD, Shea B, Wells G, et al. Fluoride therapy for osteoporosis (protocol for a Cochrane review). In: Cochrane Collaboration. *Cochrane Library*. Issue 2. Oxford: Update Software, 2000.
- 7 Riggs BL, O'Fallon WM, Lane A, Hodgson SF, Wahner HW, Muhs J, et al. Clinical trial of fluoride therapy in postmenopausal osteoporotic women: extended observations and additional analysis. *J Bone Miner Res* 1994;9:265-75.
- 8 Seeman E. Osteoporosis: trials and tribulations. *Am J Med* 1997;103(2A):74-87S.
- 9 Devogelaer JP, Nagant de Deuxchaisnes C. Fluoride therapy of type I osteoporosis. *Clin Rheumatol* 1995;14(suppl 3):26-31.
- 10 Horowitz HS. The effectiveness of community water fluoridation in the United States. *J Public Health Dent* 1996;56:253-8.
- 11 Evans DJ, Rugg-Gunn AJ, Tabari ED, Butler T. The effect of fluoridation and social class on caries experience in 5-year-old Newcastle children in 1994 compared with results over the previous 18 years. *Community Dent Health* 1996;13:5-10.
- 12 Parviainen K, Ainamo J, Nordling H. Changes in oral health from 1973 to 1982 of 13-15-year-old schoolchildren residing in three different fluoride areas in Finland. *J Dent Res* 1985;64:1253-6.
- 13 *Optimal water fluoridation: status worldwide*. Liverpool: British Fluoridation Society, 1998.

The risk of bias from omitted research

Evidence must be independently sought and free of economic interests

The rise of evidence based health care has highlighted the use of ineffective interventions, the risks of uncoordinated research, and the consequences of relying on studies published in prestigious journals while ignoring unpublished ones that have negative findings.¹⁻⁵ Systematic reviews of the best evidence are now recognised as fundamental tools in overcoming these problems because they highlight questions that need urgent answers.⁶ But is evidence based health care achieving its goals? Aren't systematic reviews which are based on existing research at risk of amplifying the irrelevant? Should we be more concerned about "bias caused by omitted research" than the well recognised pitfall of publication bias?

The increasing awareness of this danger is leading to efforts to correct this imbalance. One such attempt is the Cochrane Collaboration (an international organisation named after Archie Cochrane, the British epidemiologist), which is committed to preparing, maintaining, and disseminating systematic reviews to map the value of healthcare interventions.⁷ The public and the media are attracted to alternative medicine, while doctors, who often criticise the use of these unproved treatments, use products such as tonics, food supplements, antioxidants, memory enhancing drugs, and vasodilators for which there is no evidence that they are clinically useful. A far reaching cultural campaign is needed in Europe.

Therefore, evidence that is not only of good methodological quality but also generalisable is needed. Too often, evidence from randomised clinical trials is obtained only from selected groups of patients, and children, elderly people, and women are often excluded.^{7, 8} The use of treatments should not be extended by analogy from one group of patients to another without appropriate randomised controlled trials.

Randomised controlled trials are needed to produce generalisable evidence, and general practitioners must be involved, not just researchers. Hospital doctors can play an active part in drafting trial protocols and analysing results. The progress in cardiology achieved by the

GISSI trial in Italy as well as by the international studies on infarct survival (ISIS) for the treatment of myocardial infarction should make these trials models in terms of the example they provide of involving doctors and hospitals that are representative of different levels of the healthcare systems.^{9, 10}

To produce evidence we must work independently, free from prejudice and unfettered by the economic interests at play in medicine. It is unfortunate that the industrialised countries, especially in Europe, have delegated the control of drug trials to pharmaceutical companies. We are not suggesting that the industry is wicked, and we acknowledge its role in providing essential drugs, such as antibiotics, antitumor agents, antipsychotic drugs, and fibrinolytic agents, to name just a few. Nevertheless, delegating this responsibility places clear limitations on research, and these seem to be growing.

For economic reasons, researchers are drawn to areas likely to give the best possible financial return. This leads to a gap between public health needs and the areas on which research actually concentrates. It favours "bias by omitted research." Examples are many. Millions of people suffer from tropical diseases (malaria, leprosy, schistosomiasis), and yet no one designs realistic strategies to tackle them. Who is working to develop drugs for these diseases? The World Health Organization scrapes together a few million dollars for drug development, but the money is insufficient to develop even a single drug.

Many older drugs are marketed on the basis of what is considered poor evidence by today's standards. There are no economic incentives to improve this evidence by conducting new trials. How many antihypertensive drugs on the market have been reliably shown to reduce cardiovascular mortality in addition to lowering blood pressure? Women who have reached the menopause are given hormone replacement therapy—oestrogen or progesterone, or both—simply because indirect evidence suggests that it reduces cardiovascular mortality and fractures. And questionable