

CORRESPONDENCE

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Rosuvastatin–warfarin drug interaction

Sir—In your Oct 25 Editorial (p 1341),¹ you suggest that safety cannot be assured for statin medications, and cite the example of cerivastatin-associated rhabdomyolysis and the fact that the 80 mg dose of rosuvastatin was withdrawn by AstraZeneca because of safety concerns. I would like to highlight the clinically significant interaction between rosuvastatin and warfarin, which has received little attention to date.

The British National Formulary suggests that the effect of warfarin is “possibly enhanced” by rosuvastatin. The summary of product characteristics for rosuvastatin in Ireland suggests that concomitant administration of rosuvastatin and warfarin “may result in an increase in International Normalised Ratio (INR)” and that “appropriate monitoring of INR is desirable”. The possibility of an interaction first came to my attention from a report on an adverse event from the continuing JUPITER study, in which a 74-year-old female patient on long-term warfarin developed increased bruising, haematuria, and lightheadedness about 4 weeks after starting rosuvastatin. Her INR was recorded at 8.0, having been stable at 2.0 before the introduction of the statin. The interaction resulted in hospital admission, and treatment included the discontinuation of warfarin, 2 units fresh frozen plasma, and 10 mg vitamin K. Most clinicians would conclude that this was a clinically significant interaction.

AstraZeneca have done at least two clinical studies on the co-administration of rosuvastatin and warfarin, and presumably the results of these studies provide the basis for the suggestion by the British National Formulary that there might be an interaction between rosuvastatin and warfarin. Having received details of the studies from AstraZeneca, I am unable to outline the findings here because a confidentiality clause has been added.

Just how relevant is all this? We asked more than 1700 general practitioners in 1999 about factors they regarded as important in relation to prescription of statins. The three most important points according to the clinicians were safety, efficacy, and drug interactions. From our prescribing data in Ireland,

we estimate that there are more than 100 000 patients presently on statin treatment, and that about 10% of these patients will also be on long-term warfarin therapy. I believe your Editorial was correct in highlighting the issue of safety, and to suggest that “physicians must tell their patients the truth about rosuvastatin”. However, I would add that physicians themselves should be informed of the real risk of a clinically significant interaction between rosuvastatin and warfarin. Such a combination should be avoided in my view—alternative statin drugs can be safely co-administered.

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1 The Lancet. The statin wars: why AstraZeneca must retreat. *Lancet* 2003; **362**: 1341.

Politics in medical journals

Sir—I am dismayed by the appearance, again, of a political tract by Jerome Singh (Nov 15, p 1672),¹ this time on the necessity for rich nations to take care of poor nations. If this had been written 60 years ago, it would have been justly decried as a defence for colonialism. Justice and fairness were used as justifications then, too.

If *The Lancet* is justified in devoting a section to health and human rights—a combination that should seem odder than it does—it would be much more helpful to elaborate on the plights of the nations in reference—here Rwanda and Sierra Leone—so as to address root causes rather than pleas for alms. If political issues need to be addressed in a medical journal, surely that should start with a critical description of the corruption, lawlessness, extortion, and criminal neglect that characterise these countries. I appeal to the editors to exercise the judgment we expect in a journal of such pedigree.

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1 Singh JA. Is donor aid allocation to Iraq fair? *Lancet* 2003; **362**: 1672.

Author's reply

Sir—To extricate politics from medical journals—especially in a section dedicated to health and human rights—is wrong for at least five reasons. First, medicine has a history of being misapplied for politically motivated ends. The human rights abuses committed by physicians in the employ of the Nazi and apartheid regimes speak to this point.

Second, medical personnel sometimes practise in settings where the infliction of politically motivated human rights abuses is common. Apartheid South Africa and present-day Zimbabwe are examples of such settings.

Third, the opinion of medical professionals carries substantial moral and political clout in many quarters. If convinced on an issue, this community could use its leverage to lobby for change in policy at a state level. This strategy on AIDS treatment recently bore fruit in South Africa.

Fourth, medical professionals are involved in decision-making at the highest political levels. South Africa's Foreign Minister, for example, is a medical doctor. Cogent arguments in a reputable journal, especially when such views are endorsed by WHO,¹ could potentially influence such people to alter or affirm their state's foreign policies.

Finally, debate is healthy. It usually results in better informed individuals and policies. Medical journals, especially reputable ones, thus have an ethical duty to publish works that consider the ramifications of political decision-making on health and human rights; more so if such works can potentially realise a change in policy-making that results in ameliorations in these arenas for affected parties.

With respect to Jim Whiting's second point, I concur. Moreover, I believe that criticism of such practices—particularly given its detrimental effect on health and human rights in affected countries—should especially be voiced by those in the developing world. Although I and other colleagues from the developing world recently voiced our opinion on this issue,² more need to join our call. As we argued, corruption and self-serving aggrandisement and oppression (among

other practices) on the part of many developing world leaders is having a devastating effect on health services in those countries. Here again, medical journals have an ethical duty to publish such opinions.

Affluent donor nations are making noteworthy attempts to uplift conditions in the developing world. The Fogarty International Center of the US National Institutes of Health, for example, is a leading proponent of north-south partnerships and southern capacity-building in the medical arena. Whiting perhaps missed the point of my paper. It was not that rich donor nations are obliged to donate aid to poorer nations; rather, if they choose to do so they should disburse their aid fairly so that those most in need benefit.

Works in reputable medical journals can potentially influence policy-making and ultimately affect millions of lives. I applaud *The Lancet* for its boldness and tenacity in covering politically sensitive issues that concern health and human rights.

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- 1 Nabarro D, Loretta A, Colombo A. Increased equity in postconflict reconstruction. *Lancet* 2003; **362**: 1673.
- 2 Singh JA, Nkala B, Amuah E, Mehta N, Ahmad A. The ethics of nurse-poaching from the developing world. *Nursing Ethics* 2003; **10**: 667–71.

What are health and human rights?

Sir—The inclusion in *The Lancet* over the past several years of a regular section entitled Health and Human Rights has brought useful and timely pieces to a diverse audience, and has helped signal wider recognition of this field.

Until recently, all the pieces have in one way or another drawn out the human rights implications of health policy and practice. Although some of these pieces have been skewed towards the health effects of civil and political rights violation—in particular torture—with insufficient attention to the implication of economic and social rights for health, or the effects of attention to human rights on public health programming, all have displayed understanding of human rights principles, methods, or instruments.

All the more disappointing, therefore, to be confronted with the Health and Human Rights section in your Sept 20 and Nov 15 issues. Although the pieces are to be commended on their own merit, and each is timely and interesting,

none in fact deal with human rights but instead with social justice and ethical concerns. Those working in the fields of ethics, human rights, and social justice are learning where our fields converge, overlap, and complement one another, but our differences are also important because they define a powerful synergy, rather than redundancy, among these fields.

Traditionally, human rights issues are meant in the first instance to guide the actions of governments, whereas ethics much more broadly encompasses concern for the specific actions and relationships of individual health workers, researchers, and organisations. The ethical principles that guide our work are the product of broad-based consultation and are presented in the form of guidelines and proposed codes of conduct by professional bodies and organisations. Human rights norms and standards tend to be drafted by government representatives, negotiated in political fora, and incorporated in the body of international law in the form of international treaties which impose legal obligations on the governments that ratify them. Although each piece presented is certainly worthy of publication, I fear that their placement within this section will only serve to confuse the public health community as to the value of human rights, ethics, and social justice for public health work. Our work requires attention to the distinct value of each and the differences in the paradigms they represent. We should support these differences, but we also should not obscure them. *The Lancet*, by promoting a section entitled Health and Human Rights, also has a responsibility in this regard.

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Quality of medical education in Mexico

Sir—We agree with Julio Frenk and colleagues (Nov 15, p 1667),¹ that substantial advancements have been made in the Mexican health system. We believe that the proposed structure of the National Health Program will improve the health of the Mexican people, especially the most vulnerable.

Frenk and colleagues mention that the National Crusade of the Quality of Health Services was launched to increase the effectiveness and responsiveness of health services by

promoting the certification of health professionals and the use of clinical guidelines, and by improving access to evidenced-based resources. To achieve this end, we think that changing the way physicians are trained and taught is paramount.

According to the WHO, Mexico has 56 medical schools, from which about 7800 physicians graduate each year. This term, 21 235 physicians competed for 4625 residency spots by undergoing an examination. Results of this examination are kept private, and the general public are not informed of how medical schools rank in terms of outcome in this test. Those who are successful must apply to their hospital of preference, which then keeps their papers and makes a decision on whether or not they are accepted. This process limits the physician to applying to only one or two institutions, and needless to say benefits the institutions more than the trainees.

Residency training in Mexico is done by following a very strict hierarchical pattern, teaching is scarce, and residents learn mostly by imitation rather than evidence-based medicine. Training is done under conditions of stress, long hours of work, and poor pay.

Evidence² suggests that Mexican physicians in training are poor at critically reading clinical research. In one report, 572 residents from different specialties were assessed on their abilities to judge and interpret clinical research. Scores were low, with medians of less than 34%. 17–28% of examinees scored less than they would have if they had answered randomly.^{2,3} In another report, the level of training residents received did not affect their performance in this test.⁴ Clearly these findings cannot be applied to all Mexican medical residents, but the lack of research in this area leads us to believe that they could be a good indicator.

Furthermore, Villasis-Keever and colleagues⁵ analysed the seroprevalence of hepatitis B in residents in one institution, and concluded that only 80% had been vaccinated, of whom only 41.6% had completed the course. If these physicians do not understand the importance of preventive medicine, how can they possibly teach and practise it on their patients?

Although the main focus of Frenk and colleagues' article is based on health policies rather than education, we believe that medical education in Mexico has to be reformed, and that teaching in institutions, medical schools, and residency programmes must be standardised and certified. This standardisation will greatly improve the