Letters

Obesity association clarifies definitions of obesity and links with drug firms

EDITOR—Your reports referring to childhood obesity definitions in the USA and the International Obesity Task Force (IOTF) contained errors.[1 2] The task force is part of the International Association for the Study of Obesity (IASO), this year celebrating its 20th anniversary as the body uniting researchers, clinicians, health professionals, and others concerned with obesity worldwide.

The IOTF has no role in the childhood obesity expert group convened by the American Medical Association, the Centers for Disease Control, and the Health Resources and Services Administration. You report a proposal to adopt the 85th and 95th centiles as reference points for overweight and obesity in children. In the USA these cut-off points are termed "at risk" and "overweight."[3] Your readers may judge whether this is an effort to "expand the definition" of obesity and whether your imputation of some attempt to exaggerate the obesity problem has any foundation.

You refer to William Dietz, head of the division of nutrition and physical activity at the Centers for Disease Control, Atlanta, who served from 1998 to 2000 as the first chair of the IOTF working group on childhood obesity. This group developed the IOTF cut-off points widely used for international comparisons of childhood overweight and obesity. This approach, relating children's growth curves and cut-off points to the World Health Organization's adult body mass index criteria, was first published in the *BMJ*. It has been observed to underestimate rather than expand obesity prevalence, when compared with the standard centiles, but is not proposed for use in the USA.[4 5]

Your report made erroneous reference to the IOTF having cash amounting to more than £1m (€1.45m; $1.83m)—a sum that our annual report clearly indicated represented the combined reserves of IASO, a rapidly growing international medical organisation providing services to associations with 10 000 members in more than 50 countries, which is also seeking to meet the growing demands for engagement in many global initiatives.

Like many charitable medical societies, IASO receives income from its members, from its scientific publications, and from conference activities, and it receives occasional donations towards specific projects from pharmaceutical companies. IASO received foundation support to lead the Global Prevention Alliance, with other international non-governmental organisations concerned with obesity and related chronic diseases. We would be delighted to receive "millions" to support our work to promote strategies for the prevention of obesity, particularly among children, given the urgency and enormity of the public health challenge.

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Competing interests: NR is an employee of the International Association for the Study of Obesity.

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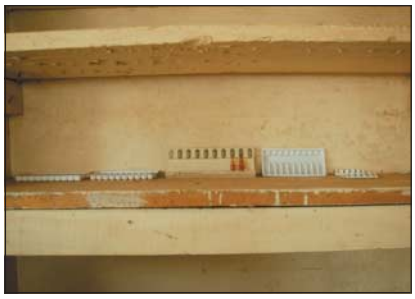
The great medicines scandal

Access is not just about cost

EDITOR—I write with reference to the editorial by Richards.[1] In addition to important information on pricing, the World Health Organization/Health Action International report provides vital information on the availability of medicines in low resource settings. The authors report alarmingly low availability of key medicines to treat chronic diseases in both public and private pharmacies across most regions.

For example, hydrochlorothiazide, considered a first line antihypertensive in many countries, had very low availability. In the private sector, median availability for the originator product and the generic product was 0% and 41%, respectively.[2] In the public sector, median availability for both products was 0%.[2] Hydrochlorothiazide remains one of the most cost effective means of controlling hypertension; but if it is not available it cannot be used. Although campaigns to reduce prices are important, they will not tackle the issue of availability.



TON KOENE/STILL PICTURES

Hospital pharmacy in the Central African Republic

The availability of beclometasone inhalers to control asthma was far below acceptable levels. The WHO/HAI report shows that no country had 100% availability of beclometasone inhalers in private sector pharmacies.[2] And only five countries showed availability of more than 30% for originator and generic beclometasone inhaler.[2] In contrast, availability of salbutamol inhalers was relatively high across most countries.[2]

These findings show that while salbutamol rescue therapy is widely used, beclometasone inhaler to prevent asthma attacks is not. This practice has implications on both outcomes and affordability.

Policies on pricing will not address the insufficient availability of chronic disease medicines. Additional qualitative and quantitative research needs to be conducted to better understand why these key medicines are not available in public and private pharmacies. Only then can interventions be designed and implemented to address availability of medicines for chronic diseases in low resource settings.

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Competing interests: None declared.

1 Richards T. The great medicines scandal. *BMJ* 2006; 332:1345-6. (10 June.)
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Next steps?

EDITOR—The recent World Health Organization-Health Action International, Europe report on disparities in price, availability, and affordability of medicines for chronic diseases is important work.[1] This entire subject matter as it relates to medicines for chronic diseases deserves wider appreciation and understanding.

It should not be allowed to be filed away on shelves to gather dust—which is a rather roundabout way of asking: "How can the contents of such a report be leveraged in effective ways?" I would suggest the following.

Firstly, teach and otherwise disseminate the contents of this report to educational institutions with courses in chronic non-communicable disease, public health, and disease management inside and outside the United States.

Secondly, encourage a dialogue between practitioners and the private sector at one or more regional or subregional meetings to discuss further the implications of this report.

Thirdly, create "access to medicines" campaigns based on existing campaigns for infectious disease medicines. Perhaps medicines for chronic non-communicable diseases require a different model?

People in resource poor countries who survive beyond their individual demographic and epidemiological transitions are already facing epidemics of diabetes and heart disease. "Access" issues regarding medicines for chronic diseases lie well under the radar for most policy makers in developing countries but these issues cannot be ignored.

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1 Richards T. The great medicines scandal. *BMJ* 2006; 332:1345-6. (10 June.)

We still need artesunate monotherapy

Editor—Seen from Geneva, the World Health Organization's "ultimatum" on artemisinin monotherapy may seem a landmark in prolonging the useful therapeutic life of the artemisinin derivatives,[1] but for the clinicians in the field, the matter is different.

In 1991 on the Thai-Myanmar border we were facing the prospect of untreatable *Plasmodium falciparum* malaria as drug resistance emerged to standard antimalarial agents. The problem was circumvented by combining artesunate or artemether with mefloquine and the development of the artemisinin combination therapy strategy. Fifteen years later the same three day regimen remains our first line therapy, but we still need artesunate monotherapy.

A prime example is highlighted in patients with uncomplicated hyperparasitaemic falciparum malaria (>4% infected red blood cells), who are at risk of severe malaria and treatment failure. These infections require a five to seven day course of treatment with oral artesunate.[2] The only alternative is parenteral quinine, which is less effective, more expensive, and less well tolerated.[3] In the second and third trimester of pregnancy, artesunate is also a better drug for uncomplicated falciparum malaria, but it needs to be given for seven days with a dose adjustment because of the altered kinetics in pregnant women.[4 5] We currently treat patients who experience a recurrence of their parasitaemia after a three day course of mefloquine-artesunate with a seven day course of artesunate combined with tetracycline or clindamycin. Obviously we would like to prescribe appropriate antimalarial therapy without the need for artesunate tablets but this is unlikely to be possible in the near future. Hence we hope that some manufacturers will continue to supply artesunate alone to be used in specific circumstances.

After resisting the change to artemisinin combination therapies, the World Health Organization is now going to the opposite extreme. Instead, it should encourage antimalarial drug manufacturers to phase out the production of single drug tablets of mefloquine (except perhaps for intermittent preventive treatment), amodiaquine, sulphadoxine-pyrimethamine, atovaquone-proguanil, and chlorproguanil-dapsone because these drugs are all we have and must be protected by fixed combination with an artemisinin derivative.

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Competing interests: None declared.

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Censorship of medical journals

Editor—I was pleased to note that the influence of commercial interests on medical publications is being taken more seriously.[1] However, another form of bias can limit the information available to doctors and scientists: the active exclusion of journals from Medline.

A year or so ago, I was asked by Dr Abram Hoffer to investigate the selection of journals to be included in Medline. A committee of internally selected experts, the Literature Selection Technical Review Committee, decides which journals to index. Since there are no definitive criteria for inclusion, the process is open to systematic bias. As a result, several journals representing areas of medicine that do not conform to the conventional paradigm have been excluded.

I invite readers to make their own judgments. Medline has rejected the following journals: *Journal of Nutritional and Environmental Medicine* (official journal of the British, Australian, and American Societies for Ecological Medicine); *Medical Veritas* (which challenges current medical practice); *Fluoride* (journal of the International Society for Fluoride Research, which contains reports on the negative aspects of water fluoridation); and *Journal of the American Physicians and Surgeons* (official journal of the Association of American Physicians and Surgeons, formally known as *Medical Sentinel*). These are in addition to the *Journal of Orthomolecular Medicine*, edited by Hoffer, which Medline has refused to index since the 1970s.

Suggestions that these journals have been excluded for not meeting quality standards, lacking scientific content, or failing to carry out full peer review might seem plausible, if all indexed journals had equally high standards. However, Medline lists publications with negligible scientific or medical content such as *Time* magazine. Under these circumstances, Medline has been unable to explain the exclusion of journals on the grounds of either scientific content or interest to the medical community.

Despite repeated questions, Medline administrators and committee members have failed to provide any assurance that their journal selection process is objective and unbiased. Exclusion of journals from Medline, simply because a selected group of experts do not "like" the subjects they cover, restricts the progress of medical science.

Lexchin and Light's paper says that "the influence of commercial interests on medical journals should be investigated systematically." This investigation could also include Medline, to try to understand the processes behind its apparent selection bias.

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Competing interests: None declared.

1 Lexchin J, Light DW. Commercial influence and the content of medical journals. *BMJ* 2006;332:1444-7. (17 June.)

Care is needed before single test results are combined

Editor—Tonelli et al have provided valuable data for those interested in the interpretation of multiple test results. I differ, however, on the question of the evaluations of interaction and risk "additivity."[1]

It seems hard to believe that the interaction between the tests is of only "modest importance" when the odds of death are altered threefold for renal impairment and twofold for proteinuria (by the presence or


IAN HOOTON/SPL

absence of the other factor.) Admittedly, these are from unadjusted figures, but this is the situation the clinician will face as it is unlikely that all the values for the adjustment factors will be available. If only some are, the full regression equation would not be appropriate. Even with the adjusted figures, the difference in odds of death still amounts to some 16%. It would be helpful to know whether the interaction term for the two tests only is significant or not.

Secondly, it is claimed in "What this study adds" that the risk estimates from the two tests are additive. Certainly, the positive likelihood ratios for the separate tests (2.1 for proteinuria and 1.57 for renal impairment) sum to 3.67, almost the positive likelihood ratio for the combined result (3.73). This result is likely to be an accident of the figures as risk combination is usually achieved by multiplication of the positive likelihood ratio for Bayesian analysis or odds ratios for logistic regression (statistical independence assumed or imposed). The product of the positive likelihood ratio is 3.3, an underestimate. The reason for this discrepancy is that the association between renal failure and proteinuria is more marked in the affected (dead) group (odds ratio 2.6) than the living (odds ratio 1.6). Care is needed before single test results are combined.

I think that there can be no substitute for empirical checking of the results of test combinations, which are available here. Regression models inevitably refer to an imaginary population with a different composition from the actual population.

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Competing interests: None declared.

1 Tonelli M, Jose P, Curhan G, Sacks F, Braunwald E, Pfeffer E. Cholesterol and Recurrent Events (CARE) Trial Investigators. Proteinuria, impaired kidney function, and adverse outcomes in people with coronary disease: analysis of a previously conducted randomised trial. *BMJ* 2006; 332:1426-9. (17 June.)

Statin guidelines should give best statin

Editor—Manuel et al show that guidelines on statin treatment should focus on people with the highest risk of coronary heart disease.[1] However, concerns about the optimal choice of statins remain.

A recent meta-analysis (n=71 108) of randomised controlled trials has shown that the occurrence of myalgia is less common with fluvastatin, pravastatin, and simvastatin than atorvastatin (odds ratio 0.28, 95% confidence interval 0.18 to 0.44; 0.43, 0.36 to 0.51; 0.23, 0.19 to 0.28; respectively).[2] This observation could also be supported by Japanese postmarketing surveys for both atorvastatin and pitavastatin.[3 4] For example, atorvastatin had an increased risk of musculoskeletal adverse events including the elevations of serum creatine phosphokinase as an important indicator of rhabdomyolysis compared with pitavastatin in Japanese common clinical practice (atorvastatin 144/4805, pitavastatin 154/7930; risk ratio 1.54, confidence interval 1.23 to 1.93; P=0.0001 by using the Mann-Whitney U test).[3 4] This difference was shown between atorvastatin and pitavastatin, although pitavastatin at 1 mg, 2 mg, 4 mg seems to be as efficacious as atorvastatin at 10 mg, 20 mg, 40 mg in the rate of reduction of low density lipoprotein cholesterol.[5] Thus, the rate of muscle related adverse events differs among statins.[2] The common shared belief is that the cause of myotoxity with statins is dose dependent.[5] We therefore think that lower doses of statin can be tolerated without the risk of muscle related adverse events.

Given that the efficacy in reducing low density lipoprotein cholesterol and cholesterol is the same respectively for atorvastatin 20 mg and 40 mg, pitavastatin 2 mg and 4 mg, rosuvastatin 2.5 mg and 10 mg, and simvastatin 40 mg and 80 mg,[2 5] lower doses of statins should be chosen in terms of optimal disease management.

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Gloomy prognoses

Represent honesty, not fear of litigation

Editor—Discussing the worst case scenario is not about avoiding litigation, but rather it is about effective communication—the imparting of information.[1] This cannot be achieved without honesty, unpleasant though this may be.

In the context of bladder cancer doctors often use the euphemisms warts, mushrooms, polyps, or trouble in the bladder when referring to the cystoscopic appearance of the tumour. Such "kindness" is misguided and can ultimately destroy trust between patient and doctor when the truth finally comes out—"If he couldn't tell me I had cancer, what else is he hiding?" Bladder "cancer" is potentially lethal, "warts" are not. Unless armed with this upsetting fact, patients cannot make the choices that are appropriate for them.

Being honest and compassionate are not mutually exclusive. There are ways of saying cancer or risk of death in a compassionate way, but at the end of the day we must be honest with ourselves and our patients. Give me an honest doctor any day rather than a kind one who dodges difficult issues.

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1 Lawson R. Gloomy prognoses keep lawyers happy but are bad for patients. *BMJ* 2006;332:1459. (17 June.)

Be neither optimistic nor pessimistic, but realistic

Editor—Neither undue optimism nor pessimism should dominate discussions with seriously ill patients and their family members.[1] Instead doctors should gravitate towards enlightened realism.

When treatment cannot be expected to work patients and their family members should be given this news in a kind and compassionate manner, free from the distraction of being asked to make an informed decision.

When treatment might help, uncertainty, expressed in a positive manner, should prevail.

"This might help, it might not. The only way to find out is to try. Since it could help, I think we should proceed. While the prognosis is not good some patients do much better than expected. Maybe your mother is in this group."

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1 Lawson R. Gloomy prognoses keep lawyers happy but are bad for patients. *BMJ* 2006;332:1459. (17 June.)

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