Editorial

A milestone, and cost effectiveness of preventive drugs

Journal of the Ceylon College of Physicians, 2010, **41**, 39

This is the second issue of the College Journal for 2010 and the first time that two issues are published. In the past years it was not an easy task to publish the Journal regularly even once a year. It was mainly due to the lack of suitable articles being submitted. After publishing the Journal regularly in 2009 and 2010, the influx of manuscripts too seems to have increased. Obvious reason is that no one would want to write to a journal that is not published regularly. A journal published once a year too is unlikely to attract authors as they would have to wait long to see their articles in print. Current issue has research papers in addition to reviews and case reports and some has been peer reviewed. The Journal will be published twice a year from now on.

It has often been said that the overarching purpose of a medical journal is to inform, interpret, criticize, integrate, influence and reform: and the individual who bears ultimate responsibility in these matters is the editor. In fact to quote Richard Smith, former editor of the *BMJ*, an editor should 'stir up, prompt debate, upset people, legitimise and set agendas". A recent paper in the *BMJ*[1] argues that despite widespread use of preventive drugs such as bisphosphonates, antihypertensives, and statins, there is no valid evidence that they represent value for money.

Large randomised clinical trials are considered to represent the strongest form of evidence in assessing whether a particular healthcare intervention works. However, little attention has been paid to the fact that people treated in these trials may not reflect the population that will receive subsequently the drug or the intervention tested in real world settings. They are tested on highly unrepresentative, freakishly ideal patients. These patients are younger than the usual real world patient, have a perfect single diagnoses, fewer other health problems. For FDA approval, you only need trials to show that the new drug is better than a placebo. But with most medical problems, we already have got some kind of treatment. So what we should be interested is whether the new drug is better than the best currently available option. So it turns out that, of all the 197 new drugs approved in the past decade, only 70% had data to show they were better than other treatments.

Earlier this year, some researchers from Finland took every patient who'd ever had a hip fracture and worked out if they would have been eligible for the trials that have been done on fracture preventing bisphosphonate drugs which are in wide use. Starting with all 7,411 fractures, 2,134 patients get excluded straight away, because they are men, and the trials have been done on women. Then from the 5,277 remaining, 3,596 get excluded because they are the wrong age: patients in the trials had to be between 65 and 79. Then, finally 609 more get excluded, because they have not got osteoporosis. This leaves 1,072 patients. So the data from the trials on these fracture preventing drugs are only strictly applicable to about one of every seven patients with a fracture. They might still work in those who have been excluded, may not work at all or may be even harmful in them. So how should we apply the trial findings to our day to day patients?

The effectiveness of treatment in the community is influenced by at least five factors – the population treated, diagnostic accuracy, provider compliance, patient adherence, and coverage of healthcare services. Population characteristics in a randomised trial, such as age and sex, generally differ considerably from that of the patient population. In the clinical setting, misdiagnosis (false positive or negative) is more likely, and this dilutes the treatment effect. Also care providers working outside a research setting may not administer the treatment faithfully. Further, the patients' other drugs may modify the effect of the treatment of interest. Finally the most important confounder is patients' compliance – in real life; patients typically take less than half of prescribed treatments whereas about 90% compliance is seen in clinical trials[2, 3]. So the cost effectiveness of an intervention in a clinical trial would be quite different to that what we would see in a real world setting, and should not be applied directly to a wide population irrespective of age, sex, co-morbidities etc. So the answer is to do true cost effectiveness trials in real life settings, once a drug has passed the stage of efficacy in randomised trials.

References

1. Jarvinen TLN, Sievanen H, et al. The true cost of pharmacological disease prevention. *BMJ* 2011; **342**: 1006-8.
2. Compston JE, Seeman E. Compliance with osteoporosis therapy is the weakest link. *Lancet* 2006; **368**: 973-4.
3. Yeaw J, Bennet IS, Sian S, Smith DB. Comparing adherence and persistence across 6 chronic medication classes. *Journal of Managed Care Pharmacy* 2009; **15**: 728-40.

Saman Gunatilake
Editor