Cost-effectiveness of high-dose atorvastatin compared with usual-dose simvastatin: less than IDEAL?

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This editorial refers to 'Cost-effectiveness of high-dose atorvastatin compared with regular dose simvastatin' by P. Lindgren et al., on page 1448

The use of statins in the management and prevention of coronary artery disease has been shown to be associated with significant reductions in the incidence of major adverse events, including death, myocardial infarction (MI), and stroke.1 Clinical practice reflects the impact of this evidence: between the EUROASPIRE I and II surveys, reported rates of statin use in Europe increased from 18.5% in 1995–96 to 57.7% in 1999–2000 among patients with coronary heart disease.2 Despite this increase, over 40% of the patients had failed to reach targeted cholesterol concentrations. Four recent trials have examined the impact of higher dose statins compared with standard dose statins in meeting more stringent low-density lipoprotein (LDL) cholesterol goals and thereby reducing cardiovascular outcomes.3 The most recent of these, the Incremental Decrease in End Points Through Aggressive Lipid Lowering (IDEAL) trial, randomized 8888 patients with a history of acute MI (AMI) to either 80 mg/day atorvastatin (the high dose treatment) or 20 mg/day simvastatin (the moderate dose treatment).4 The high dose treatment was not associated with a significant decrease in the primary outcome of a major coronary event (including death, confirmed non-fatal AMI, or cardiac arrest with resuscitation) but was associated with a reduction in secondary endpoints and non-fatal AMI.

In this article, Lindgren et al. present the results of a cost-effectiveness analysis of the IDEAL study.5 This study is important for several reasons: it is the first published economic evaluation of high-dose vs. moderate-dose statin therapy; and the first study to be conducted after the introduction of generic simvastatin. The incremental per quality adjusted life year (QALY) of shifting patients from moderate dose simvastatin to high dose atorvastatin was €47197, €62639, €35210, and €43667 in Denmark, Finland, Norway, and Sweden, respectively. Based on previously identified thresholds, the authors conclude that high-dose atorvastatin is moderately cost-effective (cost < €50 000/QALY) in three of the four countries studied.

Not surprisingly, one of the major drivers of the cost-effectiveness of high-dose atorvastatin is the price difference between the therapies, i.e. the smaller the price difference, the more cost-effective the high-dose treatment. In Finland, where the absolute difference between the prices of the two drugs was largest (€2.2 for atorvastatin 80 mg and €0.11 for simvastatin 20 mg), high dose atorvastatin was cost-effective only among high risk patients. In contrast, in Norway, the price differential was the smallest (€1.8 for atorvastatin 80 mg and €0.30 for simvastatin 20 mg) and atorvastatin appeared to be the most cost-effective. These results are consistent with the economic results of the Treating to New Targets (TNT) trial reported recently at the American College of Cardiology Meetings in New Orleans.6 The price difference of $1 between atorvastatin 80 mg and atorvastatin 10 mg was associated with an additional cost of $36 per year with the high dose treatment. However, it is estimated that substituting low-dose atorvastatin with generic simvastatin 20 mg (which became available in June 2006 in the United States) will increase the price differential between the two therapies to $2.50 and result in an increased cost of approximately $600 per year for each patient on high dose atorvastatin.

A second, and perhaps more controversial, driver of the cost-effectiveness of high-dose atorvastatin reported by Lindberg et al. is the cost associated with productivity loss due to absence from work. The authors report that absence from work was captured on the case report form in the IDEAL trial and the average salary plus employer contribution was used to estimate productivity losses. Unfortunately, there is no consensus on the valuation of these costs in the health economics literature, especially given that no treatment differences in productivity loss have been reported previously.7 A quick search of cost-effectiveness studies in AMI revealed only one study that had captured productivity costs; however, it reported the results both with and without the inclusion of these costs.8 From a societal point of view, the absence of an individual from work need not necessarily imply productivity losses if there is unemployment and another individual can fill in for the patient. The length of time that the patient is...
away from work is also important: short departures may result in the patient ‘catching up’ after returning to work, while longer departures may require the hiring of another individual. Assigning a monetary value to productivity losses is also controversial, particularly for those not in paid employment. Given the issues, it may be more appropriate to present analyses including these costs as a secondary result. It has also been suggested that both quantities (i.e. days of work lost) and the values assigned to these quantities be clearly presented, so decision makers can decide whether to include them or not. In the present study, patients in the simvastatin arm lost approximately 1.5 days more of work than patients in the atorvastatin arm, and this imposed indirect costs ranging from £177 in Finland to €379 in Denmark. Exclusion of these costs (for the reasons mentioned above) would increase the undiscounted cost per QALY associated with atorvastatin to £58121, €67303, €44424, and €50303 in Denmark, Finland, Norway and Sweden, respectively. This pushes the cost effectiveness of atorvastatin into the realm of treatments associated with a high cost per QALY in three of the four countries.

In the IDEAL trial, there was no significant difference in mortality outcomes between the two treatment arms. However, there was a statistically significant decrease in non-fatal MI and coronary revascularization in the atorvastatin arm. Using Markov modelling, Lindgren et al. estimate a survival advantage of only 0.03 QALYs (or 11 days) associated with atorvastatin treatment. Is this benefit large enough to justify the adoption of the more expensive therapy? There is a lot riding on establishing the cost-effectiveness of alternative statin therapies relative to generic simvastatin. In 2005, statin prescriptions cost the UK National Health Service (NHS) approximately £600 million. In the US, statins account for the largest drug expenditure, at $12.5 billion per year. It is very likely that these costs will be even higher in the future. The National Institute for Health and Clinical Excellence (NICE) guidance issued in early 2006 recommended that all individuals with clinical evidence of cardiovascular disease (CVD) or those with a 20% or greater risk of developing CVD within 10 years be eligible to receive statins. Based on these recommendations, it is estimated that an additional 3.3 million people will become eligible for statin therapy in the UK alone. In the USA, it is estimated that an additional 25 million should be on statin therapy and worldwide the number is as high as 175 million. This expansion in the number of patients to be treated underlines the need for finding the most cost-effective alternative.

The study by Lindgren et al. highlights the increasing importance of examining economic outcomes as part of clinical trials, especially when they involve head-to-head comparisons of active therapies. Prescription drug costs account for an increasingly larger portion of health care expenditures in the developed world. Given the fiscal constraints the health care systems operate under, many invest in health technology assessments to find the best therapy at the cheapest cost. A recent report by the NHS has predicted savings of £85 million a year if generic rather than brand name statins are prescribed. In light of the potential costs coupled with the fact that current guidelines consider LDL goals of 70 mg/dL for high risk patients ‘optional,’ the cost-effectiveness of high-dose atorvastatin compared with moderate dose simvastatin appears less than ideal to advocate a change in practice. If at a later stage, guidelines were to mandate the lower LDL goal, treatment with generic simvastatin alone would be inadequate and the need for adjunctive therapies such as ezetimibe would be required thereby changing the cost-effectiveness equation.

Conflict of interest: none declared.

References