Combination polypharmacy for cardiovascular disease prevention in men: a decision analysis and cost-effectiveness model

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study examined the cost-effectiveness of a combination of four fixed-dose medications (simvastatin, captopril, hydrochlorothiazide, and atenolol) for the prevention of primary cardiovascular disease (CVD) in men aged over 55 years without CVD, hypertension, or dyslipidaemia. This polypharmacy approach was cost-effective in comparison with no treatment. The study was generally well conducted and was based on valid methodology although some aspects of the analysis were not extensively reported. Overall, the authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to examine the cost-effectiveness of a combination of four fixed-dose medications in comparison with no treatment for the prevention of primary cardiovascular disease (CVD) in men aged over 55 years without CVD, hypertension, or dyslipidaemia.

Interventions
The four medications were simvastatin (40mg per day), captopril (12.5mg per day), hydrochlorothiazide (12.5mg per day), and atenolol (25mg per day). These drugs were combined in a single preventive strategy and compared with no treatment.

Location/setting
USA/primary care.

Methods
Analytical approach:
A Markov model was developed to simulate the long-term clinical and economic impact of the four strategies. A lifetime horizon was considered and the authors did not explicitly report a study perspective.

Effectiveness data:
The clinical data were derived from a selection of known, relevant studies, the design of which was reported only in a few instances. For example, the baseline age-specific incidence and mortality estimates for "cardiovascular accident events" came from two large observational cohorts. The treatment effect or reduction in CVD risk was mainly taken from meta-analyses, although the design of the studies included in these was not reported. In general, it appears that the authors used their judgement to select the most appropriate estimates. The key clinical input was the reduction in CVD events associated with the combined therapy.

Monetary benefit and utility valuations:
The utility valuations were derived from the literature. The utility weights were reported, but no other details were given.

Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure and were obtained from the Markov model. A 3% annual discount rate was applied.
Cost data:
The analysis considered the costs of preventive drugs, post-event acute and chronic care, and treatment of side effects. The drug costs were derived from the Red Book. All other costs were based on published reports. The details on resource use were not provided. All costs were in US dollars ($) and referred to 2003 and 2004 values. Future costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
A univariate deterministic sensitivity analysis was carried out to investigate how robust the results were to variations in key individual model inputs, which were varied by plus and minus 50%. A best-case scenario for the no treatment strategy was also considered.

Results
The combined preventive strategy resulted in total costs of $70,000 and produced 13.62 QALYs. The no treatment option resulted in total costs of $93,000 and led to 12.96 QALYs. The incremental analysis showed that the combined preventive strategy was simultaneously more effective and less expensive, in other words, it dominated the no treatment strategy.

The sensitivity analysis showed that the dominance of the preventive strategy persisted despite reasonable variations in the model inputs, even when these changes were made simultaneously in order to favour the no treatment option. Even when unrealistic values of some parameters were used, the preventive strategy was still cost-effective although no longer dominant.

Authors' conclusions
The authors concluded that a fixed-dose polypharmacy approach to prevent CVD in men aged over 55 years may be cost-effective. They stated that further research could be carried out in larger populations such as women or international groups, taking into account adherence and indirect costs.

CRD commentary
Interventions:
The choice of the comparators was appropriate. The "polypill" strategy was supported in previous reports and was compared with a strategy of starting treatment only after hypertension or dyslipidaemia had manifested. The strategy of no preventive treatment is likely to reflect the current pattern of care in several settings.

Effectiveness/benefits:
The authors selected the sources of data in order to use the best available evidence. Thus, no systematic search of sources was carried out. Some information on the design of the primary sources was given. The data were mainly based on large cohort studies or meta-analyses. Aware of the uncertainty surrounding some estimates, the authors undertook an extensive sensitivity analysis which considered reasonable ranges of values for the clinical estimates. The derivation of the benefit measure was not clearly described in terms of the methodology used to obtain the utility values which were used to calculate the QALYs.

Costs:
The authors did not explicitly state the perspective adopted, but the categories of costs appear to suggest the viewpoint of a third-party payer. Some of the sources for economic costs were reported and the most relevant costs (those related to the treatment of the disease) were derived from published studies. The transparency of the analysis was reduced for in two ways. Firstly, the costs were presented as macro-categories without a breakdown of cost items and, secondly, the methodology used to calculate costs was not described. Other aspects of the analysis such as the prices to which the costs referred and the use of discounting were reported.

Analysis and results:
The costs and benefits were synthesised in average cost-utility ratios. Incremental ratios were not required given the dominance of the preventive strategy. The issue of uncertainty was restricted to a deterministic approach, but the assessment of a best-case scenario was appropriate in investigating the conditions under which the less favourable
strategy would be preferred. Nevertheless, it turned out that the preventive strategy remained the most cost-effective. The authors acknowledged that non-adherence was not considered, although it might be an issue in real-world settings. The results should be considered specific to the authors’ setting as differences might exist in the baseline risk of CVD between the US population and that of other countries (mainly in terms of the prevalence of obesity).

Concluding remarks:
The study was generally well conducted and was based on valid methodology, although some aspects of the analysis were not extensively reported. Overall, the authors’ conclusions appear to be valid.

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