Cardiovascular disease prevention with a multidrug regimen in the developing world: a cost-effectiveness analysis
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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 two four-drug regimens for the primary and secondary prevention of cardiovascular disease in low- and middle-income countries. The authors concluded that the combination therapies reduced the risk of death from cardiovascular disease and were cost-effective, especially in high-risk patients. The methods were valid, which enhances the reliability of the authors’ conclusions, despite limited reporting of the data sources.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of two four-drug regimens for the primary and secondary prevention of cardiovascular disease, in low- and middle-income countries.

Interventions
The two regimens of generic drugs were based on the World Health Organization (WHO)’s list of essential drugs to treat and prevent cardiovascular disease. The background comparator was no treatment.

The primary prevention regimen was given to patients without a history of cardiovascular disease and consisted of aspirin, a statin, an angiotensin-converting enzyme inhibitor, and a calcium-channel blocker. The doses were 81mg aspirin, 40mg lovastatin, 10mg lisinopril, and 5mg amlodipine. Patients at four different 10-year absolute risks of cardiovascular disease (5%, 15%, 25%, and 35%) and those older than 55 years with or without any additional risk factor were considered.

The secondary prevention regimen was given to patients with a history of cardiovascular disease and consisted of aspirin, a statin, an angiotensin-converting enzyme inhibitor, and a beta-blocker. The doses were the same, except that metoprolol was substituted for amlodipine.

Location/setting
The six low- and middle-income regions, defined by the World Bank (East Asia and Pacific, Eastern Europe and central Asia, Latin America and Caribbean, Middle East and north Africa, South Asia, and sub-Saharan Africa)/primary care.

Methods
Analytical approach:
The analysis was based on a Markov model, with a lifetime horizon. The authors stated that a societal perspective was adopted.

Effectiveness data:
The clinical data were from a selection of relevant sources, which included high-quality studies, such as published meta-analyses for primary prevention and clinical trials for secondary prevention. The details of these sources were presented in an online appendix. The disease progression was based on Framingham equations. The key input for the model was the relative-risk reduction in cardiovascular disease-related events (death, ischaemic heart disease, and stroke), with the
Monetary benefit and utility valuations:
The utility values were from the Disability Weights of the WHO Global Burden of Disease project, which was produced by more than 350 experts worldwide, who investigated various interventions to reduce the burden of disease in developing countries.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at an annual rate of 3%.

Cost data:
The economic analysis included the costs of drugs, screening, monitoring, and treatment of cardiovascular disease events (myocardial infarction, stroke, re-infarction, and long-term care). These included personnel, health care visits, diagnostic tests, and hospital stay, which were based on WHO estimates for the six defined regions. The drug costs were from the International Drug Price Indicator Guide. All costs were in US dollars ($), the price year was 2001, and a 3% annual discount rate was applied.

Analysis of uncertainty:
One-way sensitivity analyses were undertaken to examine the impact of variations in the model inputs on the cost-utility ratios, using published ranges of values for the clinical inputs and a range of half to double for the reported costs. Three alternative scenarios were considered: aspirin was excluded from the primary prevention regimen; the drug efficacy was halved; and different assumptions for the possible overestimation of up to 20% of the Framingham risk function were examined. A probabilistic multivariate sensitivity analysis, based on a Monte Carlo simulation, was carried out focusing on the assumption of the relative risks for the drug efficacies.

Results
Compared with no treatment, the incremental cost per QALY gained with primary prevention ranged in the six regions from $746 to $890 for patients with a 10-year absolute risk of 25% or more; from $790 to $930 with a 10-year absolute risk of 15% or more; and from $1,039 to $1,221 with a 10-year absolute risk of 5% or more. These ratios were all below the threshold of three times the gross national income per person by region, recommended by the WHO (range $1,320 to $11,010).

Primary prevention for those older than 55 years and for those with a 10-year absolute risk of 35% or more, was weakly dominated as it was more costly and had a higher incremental cost-effectiveness ratio than the next more expensive strategy.

Compared with no treatment, the incremental cost per QALY gained with secondary prevention ranged in the six regions from $306 to $388.

The sensitivity analysis showed that the drug efficacy was the most sensitive parameter, but the results remained generally stable; the cost-effective strategies remained cost-effective and the order of alternatives did not change.

Authors’ conclusions
The authors concluded that the combination therapies reduced the risk of death from cardiovascular disease and were cost-effective, especially in high-risk patients.

CRD commentary
Interventions:
The authors provided an extensive justification for their selection of the comparators, which appear to have been appropriately chosen. Two different regimens were considered for primary and secondary prevention.

Effectiveness/benefits:
The clinical data were from valid sources that included a meta-analysis and clinical trials, but no further details of these
sources were provided and the method used to identify them was not reported. More details might have been available from the online appendix. The disease progression was based on a common risk function (Framingham equations). The authors stated that this function might overestimate the cardiovascular risk and this was tested in the sensitivity analysis. QALYs were an appropriate benefit measure given the impact of the disease on both survival and quality of life. The utility weights were from a valid source, but the instrument used to elicit the preferences was not stated.

Costs:
The authors stated that a societal perspective was adopted, but productivity costs and non-medical direct costs were not included. Other items, such as hospital costs for acute cardiovascular events, were excluded on the assumption of limited availability for admission in most developing countries, but this assumption was tested in the sensitivity analysis. The unit costs and resource use were presented for drugs, screening, and laboratory tests, while other items were presented as category totals only. The sources of costs and resource use appear to have been appropriate, but were only partly described. Most of the costs were varied in the sensitivity analysis.

Analysis and results:
The results were clearly presented, but only the incremental findings (interventions minus no treatment) were reported in the text, with the costs and QALYs presented in graphs. Incremental ratios were appropriately calculated to synthesise the costs and benefits of the alternative strategies. The uncertainty was satisfactorily investigated using various approaches. The study focused on developing countries with low or middle-incomes and cannot be generalised to developed countries.

Concluding remarks:
The methods were valid, which enhances the reliability of the authors’ conclusions, despite limited reporting of the data sources.

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