Plant stanol esters are potentially cost-effective in the prevention of coronary heart disease in men: Bayesian modelling approach
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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.

Health technology
The study investigated the use of plant stanol esters incorporated in spreads in the prevention of coronary heart disease (CHD), with and without treatment with 3-hydroxy-3-methylglutaryl coenzyme A inhibitors (statins). This intervention was compared with a normal daily diet.

Type of intervention
Primary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of men and women aged between 30 and 60 years and without established CHD.

Setting
The intervention was a commercial product. The economic study was set in Finland.

Dates to which data relate
The effectiveness data were derived from studies published between 1994 and 2002. The resource use data were derived from studies published between 1994 and 2003. The price year was 2001.

Source of effectiveness data
The epidemiological data used in the economic analysis included:

- the prevalence of risk factors for CHD (e.g. blood pressure, cholesterol levels, smoking, diabetes), and
- the annual risk of non-CHD deaths, CHD nonfatal events and CHD deaths.

The effectiveness data corresponded to the total cholesterol reductions obtained with plant stanol ester-containing spreads and for the combination of plant stanol ester-containing spreads and statin drug treatment.

Modelling
A discrete-state, discrete-time Markov model was used to estimate the expected costs and health outcomes. The structure of the Markov model was based on a published article (Cook et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details). The time horizon was until death or 100 years.
Sources searched to identify primary studies
The effectiveness data were derived from two systematic literature reviews. The first meta-analysis included 19 randomised trials evaluating the effectiveness of plant stanol esters in spread. The second meta-analysis included 5 trials evaluating the effectiveness of plant stanol esters added to spreads in combination with statin treatment. Risk factor and mortality data were derived from Finnish datasets.

Methods used to judge relevance and validity, and for extracting data
The authors reported that two systematic reviews of the literature were conducted for the main effectiveness estimate. Trials were identified from MEDLINE and the Cochrane Library and previous review articles. The reviews included all randomised placebo-controlled trials, either parallel or crossover in design. Studies were excluded if free stanols or products other than spread were used, or the participants were children or had ileostoma. The remaining studies were combined using a meta-analysis.

Measure of benefits used in the economic analysis
The measure of health benefits used was the quality-adjusted life-years (QALYs). Age- and gender-specific utility values were derived from a Finnish EQ-5D survey (n=2,374). Disutility arising from CHD events was derived from a published Finnish study. The QALYs were discounted at an annual rate of 3.5% in the base-case.

Direct costs
The direct costs included in the analysis were those of the health care system and patients. They included the costs of hospitalisation and outpatient care, medication and stanol ester spread. Hospitalisation and outpatient costs were based on a sample of 9,226 Finnish patients. The costs of medication were obtained from the National Agency for Medicines and the Social Insurance Institution’s databases. The costs of spreads (both plant and regular) were obtained from a survey by the Finnish Consumer Agency. Since the costs could be incurred over the lifetime of the patient, discounting was relevant and was appropriately performed at an annual rate of 3.5%, as recommended in current guidelines. The study reported the average costs. The price year was 2001.

Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
Although the authors reported that a societal perspective was used in the analysis, productivity costs and other indirect costs were not included.

Currency
Euros (EUR).

Sensitivity analysis
The authors performed a series of one-way sensitivity analyses by varying the discount rate, gender and age composition of the patients. In addition, a Monte-Carlo simulation using 10,000 samples was performed, with the first 2,000 simulations being discarded to ensure stability. To illustrate decision uncertainty, the authors constructed cost-effectiveness acceptability curves.

Estimated benefits used in the economic analysis
The authors did not report the average number of QALYs gained and only reported the incremental cost-utility ratios.
Cost results
From a health care system perspective (excluding the costs of the spread), the discounted lifetime cost-savings ranged from EUR 20.4 to EUR 124.0 per patient.

Synthesis of costs and benefits
The costs and benefits were combined using an incremental cost-utility ratio (the additional cost per QALY gained).

For men, the additional cost per QALY gained when plant stanol ester-containing spread was compared with normal diet ranged from EUR 10,106 to EUR 71,436. In women, the incremental cost-utility ratios ranged from EUR 34,327 to EUR 112,151 per QALY gained.

The results of the sensitivity analysis showed that for men, when the cost per QALY threshold was EUR 30,000, the probability of plant stanol ester-containing spread being cost-effective was over 90%. In women, for those aged 50 years or younger, there was a probability of less than 15% that plant stanol ester-containing spreads were cost-effective, whereas at age 60 years or older there was a probability of over 90% that they were cost-effective.

Authors' conclusions
Based on the results, plant stanol esters incorporated in spreads could be viewed as cost-effective in the prevention of coronary heart disease (CHD) in adult males and in older age groups of women.

CRD COMMENTARY - Selection of comparators
A justification was given for using a regular spread as the comparator. It represented current practice in the authors' settings. You should decide if the comparator used represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The parameters were derived from published data. The authors performed two meta-analyses based on the results from a review of the literature. They reported the search methods, inclusion criteria and the primary end points of the review in detail. The effectiveness parameters were derived from meta-analyses based on randomised controlled trials, which have the greatest level of internal validity.

Validity of estimate of measure of benefit
The estimation of health benefit (QALYs) was derived appropriately using a Markov model. The QALYs gained were appropriately discounted. The utility values were derived from a large Finnish sample and from published studies that used the EQ-5D.

Validity of estimate of costs
The authors reported that the study had been conducted from a societal perspective, but productivity costs were not included. From a health care system perspective it would appear that all the major relevant costs were included in the analysis. The costs were derived from published sources. Since the costs could be incurred over the lifetime of the patient, discounting was relevant and was appropriately performed. The authors only reported the costs to the health care system and did not include the costs of the spreads when they reported average costs. The price year was reported, which will aid any future inflation exercises.

Other issues
The authors reported that the cost-effectiveness of plant stanol and sterol esters remains unevaluated. They also reported that the results might not be generalisable to other settings as the study was based on a Finnish health care setting. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.

Implications of the study
The authors appear to recommend the use of plant stanol esters in spreads for all adult males.
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Other publications of related interest
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Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Aged; Bayes Theorem; Biomarkers /blood; Cholesterol /blood; Coronary Disease /blood /economics /epidemiology /prevention & control; Cost-Benefit Analysis; Female; Finland /epidemiology; Humans; Male; Markov Chains; Middle Aged; Phytotherapy /economics; Plant Preparations /economics; Quality of Life; Quality-Adjusted Life Years; Randomized Controlled Trials as Topic; Risk Factors; Sitosterols /economics /therapeutic use; Treatment Outcome; Uncertainty

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