Cost-effectiveness of adding prolonged-release nicotinic acid in statin-treated patients who achieve LDL cholesterol goals but remain at risk due to low HDL cholesterol: a UK-based economic evaluation
Roze S, Wierzbicki A S, Liens D, Renaudin C

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 examined the addition of prolonged-release nicotinic acid (PR NA) (1,000 mg daily) to statin therapy in order to raise high-density lipoprotein (HDL) cholesterol levels and to reduce the risk of cardiovascular disease (CVD) in statin-treated patients with low HDL.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of statin-treated patients with HDL cholesterol <1.0 mmol/L and LDL cholesterol <3 mmol/L. Patient with diabetes were excluded in the base-case.

Setting
The setting was primary care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness data were derived from studies published between 1999 and 2006. The costs and resource use data were derived from studies published between 2002 and 2004. The price year was 2005.

Source of effectiveness data
The clinical data used in the model were the baseline characteristics of the patients, the treatment effect for statin and the effect of PR NA.

Modelling
Two analytic decision sub-models were developed to project the long-term clinical and economic outcomes of treating a cohort of 2,000 hypothetical patients with dyslipidaemia.

The first sub-model was based on a second-order Monte Carlo simulation to determine lipid levels after treatment with statins in a dyslipidaemic population. Patients with HDL cholesterol <1.0 mmol/L and LDL cholesterol <3 mmol/L entered the second sub-model and could receive standard statin therapy or PR NA plus statins.

The second sub-model was a standard Markov model, based on risk estimates from the Framingham study, to evaluate
the long-term cumulative incidence of coronary heart disease (CHD) events (angina, myocardial infarction and CHD death). The structure of the model was presented graphically and the main health states were described. The simulation was run for 40 years. The authors stated that full details of the economic model were given in a separate study (Roze et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details).

Sources searched to identify primary studies
The baseline characteristics of the patients and the statin treatment effect were derived from the Heart Protection Study. The effectiveness of PR NA in raising HDL was obtained from the ARBITER 2 study. The authors did not provide details of these two sources of data, but baseline characteristics for the patient population of the Heart Protection Study were presented. Disease progression (transition probabilities) was based on the Framingham study.

Methods used to judge relevance and validity, and for extracting data
It was unclear whether a systematic review of the literature was undertaken to identify the primary studies. The studies may therefore have been identified selectively. No reasons for choosing these studies were given, but the use of Framingham equations to model disease progression and risk for CVD represents a standard approach.

Measure of benefits used in the economic analysis
The summary benefit measures used were the life-years (LYs) and quality-adjusted life-years (QALYs). The utility weights used to calculate QALYs were derived from two reports submitted to the National Institute for Health and Clinical Excellence (NICE). No details of the instruments used to obtain utility weights were given. The benefits were discounted at an annual rate of 3.5%.

Direct costs
The analysis of the costs was performed from the perspective of the NHS. It included the costs of PR NA and the treatment of CHD complications (myocardial infarction and/or angina). These costs included resources associated with hospital stay, day case admissions and outpatient visits. The unit costs and the resource quantities were not presented separately, except for PR NA acquisition cost. The costs and resource use were estimated using data derived from two reports submitted to NICE in 2002 and 2004 that used resource use data from the 1998 cohort of the Nottingham Heart Attack Register. The price year was 2005.

Statistical analysis of costs
The costs and quantities were treated deterministically.

Indirect Costs
Productivity costs were not included given the perspective of the study.

Currency
UK pounds sterling (€).

Sensitivity analysis
A univariate sensitivity analysis was carried out to evaluate the impact on the cost-effectiveness ratios of changes in the variables. Such variables included the efficacy of PR NA (+/- 20%), the cost of cardiovascular complications (+/- 30%), discount rates (6% or 0%), the average age (+/- 10 years) and gender distribution of the population (50 to 100% male), and the HDL cholesterol target value (1.2 mmol/L instead of 1.0 mmol/L). A further simulation was also performed based on the characteristics of the diabetes sub-group of the Heart Protection Study (29% of the study population).
**Estimated benefits used in the economic analysis**
The expected LYs were 12.41 with statin monotherapy and 12.59 for PR NA added to statin therapy (difference 0.1798).

The expected QALYs were 9.86 with statin monotherapy and 10.00 for PR NA added to statin therapy (difference 0.1384).

**Cost results**
The total costs were 20,482 with statin monotherapy and 23,377 for PR NA added to statin therapy (difference 2,895).

**Synthesis of costs and benefits**
The costs and benefits were combined by calculating incremental cost-effectiveness ratios and cost-utility ratios.

The incremental cost per LY gained with PR NA added to statin therapy over statin monotherapy was 16,101.

The incremental cost per QALY gained with PR NA added to statin therapy over statin monotherapy was 20,915.

The sensitivity analysis showed that the base-case results were robust to variations in key clinical and economic inputs. In all cases the incremental cost per LY gained was lower than 20,000. A substantial reduction in the cost per LY gained was achieved when the analysis was carried out in a cohort of patients at higher risk, such as patients with a history of diabetes. In this case, the cost per LY gained with PR NA added to statin therapy was 9,568.

**Authors’ conclusions**
The addition of prolonged-release nicotinic acid (PR NA) to statin therapy for the treatment of dyslipidaemia was a cost-effective strategy in comparison with statin monotherapy. PR NA was particularly cost-effective in the sub-group of diabetic patients.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparator was appropriate as statin monotherapy represented the current pattern of care for patients with dyslipidaemia. You should decide whether this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The primary studies used to populate the decision model were presumably identified selectively. In effect, the authors did not report the methods and conduct of a systematic review of the literature. Few details of the primary studies were reported, which limits the possibility of assessing the validity of the primary sources. However, the efficacy data came mainly from a randomised controlled trial, which should ensure high internal validity. In addition, the uncertainty around the key clinical input (efficacy of PR NA) was investigated in a univariate sensitivity analysis.

**Validity of estimate of measure of benefit**
Both LYs and QALYs are appropriate summary benefit measures since they capture the impact of the intervention on survival and quality of life, which are relevant dimensions of health for patients with dyslipidaemia. The approach used to estimate the utility weights was described in part as these values were taken from a published paper. However, no other details were provided. Discounting was performed in accordance with UK guidelines and the impact of using an alternative discount rate or no discounting was investigated.

**Validity of estimate of costs**
The categories of costs included were consistent with the perspective adopted in the study. However, only macro-categories were provided and cost items were not broken down for each category. This might limit the possibility of replicating the analysis in other settings. The information on the costs and quantities of resource use was limited as the
cost estimates were taken from two reports submitted to NICE. Statistical analyses of the costs and quantities were not performed. The impact of changing some key costs was investigated in the sensitivity analysis. The price year was reported, which will facilitate reflation exercises in other time periods.

**Other issues**
The authors stated that the cost-effectiveness of PR NA had also been demonstrated in other countries. The issue of the generalisability of the study results to other settings was not explicitly addressed, but sensitivity analyses were used to investigate the impact of changes in key clinical and economic assumptions. This improves the external validity of the analysis. The results of the economic evaluation were presented clearly.

**Implications of the study**
The study results support the routine use of PR NA added to statin therapy for the treatment of dyslipidaemia. This appears to be important for the UK as a high prevalence of statin-treated patients with low HDL was found.

**Source of funding**
Funded by a grant from Merck KGaA.

**Bibliographic details**

**Other publications of related interest**
Because readers are likely to encounter and assess individual publications, NHS EED abstracts reflect the original publication as it is written, as a stand-alone paper. Where NHS EED abstractors are able to identify positively that a publication is significantly linked to or informed by other publications, these will be referenced in the text of the abstract and their bibliographic details recorded here for information.


**Indexing Status**
Subject indexing assigned by CRD

**MeSH**
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