Cost-effectiveness of varenicline compared with bupropion, NRT, and nortriptyline for smoking cessation in the Netherlands
Hoogendoorn M, Welsing P, Rutter-van Molken M P

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 long-term cost-effectiveness of varenicline to support smoking cessation in comparison with no treatment, bupropion, nortriptyline, or nicotine-replacement therapy (NRT). The authors concluded that varenicline was cost-effective compared with nortriptyline and unaided cessation, and was cost-saving compared with bupropion and NRT. The study was based on valid methodology, but some data sources were not extensively reported. The uncertainty was investigated in depth, which enhances the validity of the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study examined the long-term cost-effectiveness of varenicline, a new pharmacotherapy to support smoking cessation, in comparison with no treatment, bupropion, nortriptyline, or nicotine replacement therapy (NRT). Only adults were considered.

Interventions
The interventions were varenicline, bupropion, nortriptyline, NRT, and no intervention or unaided cessation.

Location/setting
Netherlands/primary care.

Methods
Analytical approach:
This economic evaluation was based on a published probabilistic decision model, namely the Benefits of Smoking Cessation on Outcomes (BENESCO) study. The model had a lifetime horizon. The authors stated that the analysis was carried out from the perspective of the Dutch health care payer.

Effectiveness data:
The clinical data came from a selection of known, relevant, Dutch studies, whenever possible. Two clinical trials were used to derive the abstinence rates associated with varenicline relative to bupropion and placebo. The treatment effects for the other interventions were derived from a Cochrane review. The studies included in this review were not reported. Indirect comparisons were made using placebo as the common comparator. The key clinical endpoint was the cessation rate at 12 months.

Monetary benefit and utility valuations:
The utility valuations associated with specific health states came from a Dutch study, in which preferences were elicited from the general population.

Measure of benefit:
The summary benefit measures were the number of quitters, life-years (LYs), and quality-adjusted life-years (QALYs). These benefits were discounted at an annual rate of 1.5%.

Cost data:
The economic analysis included the costs of the interventions (counselling time, consultation time with a general practitioner prescribing the medication, and medications) and the medical costs associated with smoking-related diseases (chronic obstructive pulmonary disease, coronary heart disease, stroke, and severe asthma). The costs were presented as macro-categories and only the intervention costs were broken down. The sources of costs were not explicitly reported, but all costs were taken from published studies. Costs were in Euros (EUR) and were discounted at an annual rate of 4%. The price year was 2004.

Analysis of uncertainty:
Both probabilistic and deterministic one-way sensitivity analyses were carried out. The former was based on a second-order Monte Carlo simulation that assigned probability distributions to all the model inputs. The latter used alternative sources of values for the clinical inputs, applied various discount rates (or no discounting), excluded the effect of smoking on asthma exacerbations, reduced the time horizon to 20 years, excluded the baseline prevalence of smoking-related disease, and assumed that the relative risk of smoking-related disease for long-term quitters was equal to that of former smokers rather than never smokers.

Results
In a population of 884,000 potential quitters, in comparison with no intervention, the expected LYs gained were 79,900 with varenicline; 55,100 with bupropion; 47,800 with nortriptyline; and 44,900 with NRT. The QALYs were 121,900 with varenicline; 84,100 with bupropion; 72,900 with nortriptyline; and 68,400 with NRT.

The additional intervention costs, in millions, over no intervention were EUR 338.7 with varenicline; EUR 289.8 with bupropion; EUR 137.5 with nortriptyline; EUR 285.8 with NRT. The savings from prevented diseases, in millions, were EUR 299.2 with varenicline; EUR 206.4 with bupropion; EUR 178.8 with nortriptyline; EUR 168.0 with NRT.

In comparison with no intervention, the incremental cost per QALY gained was EUR 320 with varenicline, EUR 990 with bupropion, EUR 1,720 with NRT, while nortriptyline was dominant which means it was less expensive and more effective. Varenicline was cost-saving compared with bupropion and NRT, and its incremental cost per QALY over nortriptyline was EUR 1,650.

The results of both the deterministic and the probabilistic sensitivity analysis confirmed that the base-case findings were robust. Varenicline dominated bupropion in 75% and NRT in 78% of the simulations. Above the willingness to pay threshold of EUR 5,000 per QALY gained, the probability of varenicline being cost-effective was around 84% compared with bupropion, NRT, and unaided cessation, while in comparison with nortriptyline, the probability was 70% at a threshold of EUR 20,000 per QALY. The most influential model inputs were the time horizon, discount rate, and assumptions about the relative risk of disease for long-term quitters.

Authors’ conclusions
The authors concluded that varenicline was cost-effective in comparison with nortriptyline and unaided cessation, and was cost-saving compared with bupropion and NRT.

CRD commentary
Interventions:
The selection of the comparators appears to have been appropriate in that all the available pharmacologic strategies were considered and no treatment was the background comparator.

Effectiveness/benefits:
The identification of the clinical sources of data was based on the authors’ knowledge of available country-specific sources. No systematic search appears to have been carried out. The treatment effect was derived from clinical trials for varenicline versus bupropion or placebo and from a Cochrane review for the other treatments. Indirect comparisons were used due to the lack of head-to-head comparisons. In general, the sources appear to have been appropriate and valid, although little information was given on their design and patient populations. Only a few details on the derivation of the utility estimates were presented. Both disease-specific (quit rates) and generic (LYs and QALYs) benefit measures were used, which was appropriate and makes the findings relevant to different decision makers or health care professionals. LYs and QALYs also allow comparisons to be made with the benefits of other health care
interventions.

Costs:
The cost categories reflected the perspective. The intervention costs were broken down in individual cost items, but the disease costs were presented as macro-categories, which reduces the transparency of the economic analysis. The sources of costs were not clearly described, but the price year and the use of discounting were reported. The sensitivity analysis did not investigate the effect of variations in individual cost items, but these were tested together in the probabilistic analysis.

Analysis and results:
The use of an incremental approach to combine the costs and benefits was appropriate and the findings were clearly presented. In general, the issue of uncertainty was satisfactorily addressed using two valid approaches, the methods and conduct of which were clearly described. For example, the type of probability distribution attributed to each category of model input was reported. The authors pointed out that the study results should be conservative for varenicline as only the direct costs were included, passive smoking was not accounted for, and some diseases associated with smoking were not considered.

Concluding remarks:
The study was based on valid methodology, but some sources of data were not extensively reported. The uncertainty was investigated in depth, which enhances the validity of the authors’ conclusions.

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