NHS
Centre for Smoking Cessation and Training

Cost-effectiveness of pharmacotherapy for smoking cessation

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Executive Summary

Cost-effectiveness analysis, even with its inherent methodological problems, consistently shows that when smoking cessation interventions are effective they are invariably also cost-effective. This is largely due to their relative low cost and the big impact that stopping smoking has on health outcomes. This is also the case for pharmacotherapy for smoking cessation, including nicotine replacement therapy (NRT), bupropion (Zyban) and varenicline (Champix).

There is evidence that varenicline may be more cost-effective than other pharmacotherapy. Evidence is less conclusive about the relative cost-effectiveness of NRT compared with bupropion. Combination therapy (several forms of NRT, or NRT and bupropion) is also cost-effective compared with brief advice or counselling alone. While it is likely that combination pharmacotherapy, as compared with mono-pharmacotherapy, is cost-effective it has not yet been directly evaluated.

Findings from economic analyses from the UK and elsewhere confirm that smoking cessation interventions, including pharmacotherapy, are among the most cost-effective health care interventions available.

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Key points

1. Cost-effectiveness overview

1.1 Definitions and methodology

- Cost-effectiveness compares the impact of two or more alternative courses of action with regards to their costs and benefits. Within the health care setting such cost-effectiveness analysis (CEA) usually focuses on the additional cost per additional unit of health gain created by one compared with another intervention: the incremental cost-effectiveness ratio (ICER).[1]
- In contrast to cost benefit analyses, where health-related consequences are expressed in monetary terms, CEA uses either life-years (LY) or quality adjusted life years (QALY) gained.[2] The former simply counts the additional years added to a person's life due to an intervention, while the latter weights these years according to the perceived life quality in terms of a number of factors such as pain / discomfort, mobility and mental well-being.[3] Each QALY is assigned a value between 1.0 (perfect health) and 0.0 (death). However, in smoking cessation research CEA values greater than 1.0 have been applied as stopping smoking not only reduces mortality but also chronic morbidity; thus a chronic morbidity component has been added.[4]
- CEA additionally takes into consideration the fact that the worth of extended life in the future is considered to be less than if immediately realised, due to the uncertainties we associate with future events.[5] Each LY or QALY is therefore discounted by a fixed amount per year, typically between 1.5% – 3.5%.[6]

1.2 NICE Guidance

- The National Institute for Health and Clinical Excellence (NICE) is charged with evaluating the effectiveness as well as cost-effectiveness of treatments in order to make recommendations about the implementation in the UK National Health Service (NHS).[7]
- NICE has adopted a cost-effectiveness threshold of £20,000 – £30,000 per QALY above which interventions are unlikely to be recommended. However, there is much debate about the correct level of this threshold which is considered implicit rather than explicit[8] and varies enormously between countries.[9] In fact, in NHS settings the cost-effectiveness threshold for circulatory diseases and cancers is below £20,000[10], whilst NICE recommendations in practice have a much higher threshold.[11]

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1.3 Caveats

- CEA is ubiquitously used by decision makers. However, there are considerable differences in outcomes of CEA due to the various assumptions necessary to predict future health benefits.[12]
- There are four main problems of CEA that need to be borne in mind when interpreting results.[2,13]

  1) QALY: can health be adequately expressed in economic terms at all? Methods require that subjective ratings from many people are aggregated into a single measure.

  2) Costs / uncertainty: how should intersectoral, wider societal costs be evaluated? It is likely that an intervention may have unintended positive or negative costs not considered.

  3) Discounting: what is the right threshold? Higher rates will favour acute interventions over preventative interventions and thus put more value on treatments for the elderly.

  4) Equity: how can the needs of different patient populations (e.g. those from lower socio-economic groups, those with greater clinical need) be accurately captured? Differential weighting of costs by QALY for different populations may be applied.

2. Cost-effectiveness of single pharmacotherapy

There are three principal forms of pharmacotherapy available on prescription for smoking cessation in the UK.

2.1 Nicotine Replacement Therapy (NRT)

- NRT delivers nicotine either through the skin, nasal or buccal mucosa to reduce cravings and withdrawal symptoms, and the rewarding effects of smoking as well as providing some behavioural control.[14] It is available in seven forms (gum, patch, inhaler, lozenge, sublingual tablet, nasal or mouth spray). NRT has been found to be very effective, roughly doubling a smoker's chances of remaining abstinent.[15]
- The cost per quitter for brief advice and NRT has been estimated between £267 in 1997[16] and £649 in 1999.[17] Most recently, in 2002, the cost per lifetime quitter was put between £1,173 and £2,288.[18] Cost-effectiveness estimates in the UK vary equally widely for NRT with ICER ranging more than 10-fold from £350 in 1998[19] to £4,500 per LYS in 1994[20] compared with brief GP advice alone; estimates from the US are similarly diverse.[4] The ICER of NRT was estimated in 2002 to range between £494 and £3,554 per QALY depending on the comparator and assumptions for QALY saved (see Figure 1).[18] Despite this range in estimates, all CEA conclude that NRT is highly cost-effective and this is reflected in NICE guidance.[21]

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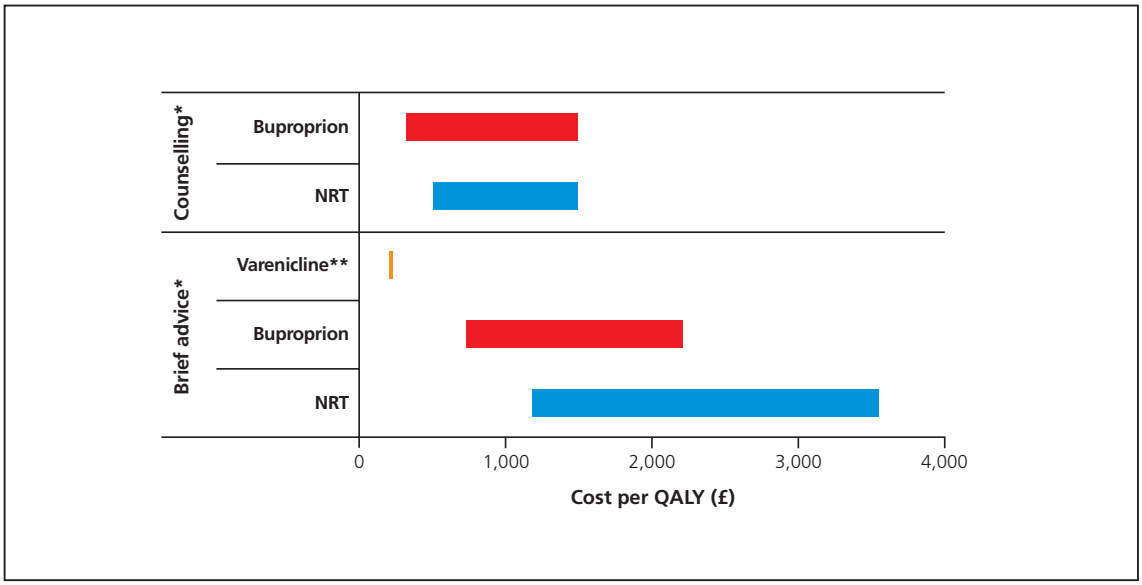
Figure 1: Incremental cost effectiveness ratio of pharmacotherapy and brief advice or counselling compared with brief advice or counselling alone.



***Comparator; **Based on one study only**[22]
Please note where appropriate prices have been converted to GBP

2.2 Bupropion (Zyban)

- Bupropion is an atypical antidepressant which acts on dopamine and noradrenaline pathways and possibly as a nicotinic antagonist, thus reducing withdrawal symptoms and the rewarding effects of smoking.[23] Bupropion is a very effective smoking cessation aid, increasing smoking cessation rates by around 70% compared with placebo.[24]

- In the UK, the cost per life-time quitter for bupropion has been estimated at between £964 and £1,799 in 2002,[18] roughly equivalent to the costs in the US.[25] The ICER of bupropion is equally favourable, estimated at around £830 per QALY in the US in 2005 compared with brief advice.[26] In the UK, this figure varies between £316 and £2,212 depending on the comparator and assumptions (see Figure 1). There is also some evidence that bupropion is more cost-effective than NRT when considering the ICER of these interventions[27] and in direct comparison (see Figure 2).[28] These results need to be interpreted with caution, however, as this was only observed in comparison with the nicotine patch, not gum, and was derived from different countries so may therefore not straightforwardly translate to the UK. It is clear, however, that bupropion is very cost-effective and is therefore recommended as a first-line treatment by NICE guidelines.

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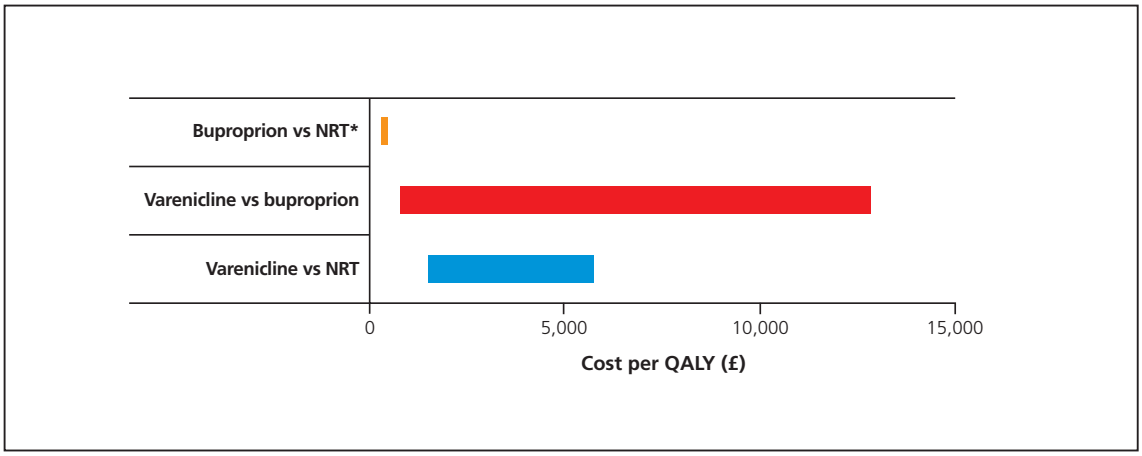
Figure 2: Incremental cost effectiveness ratios between different pharmacotherapy.



***Based on one study only**[28]
Please note where appropriate prices have been converted to GBP

2.3 Varenicline (Champix)

- Varenicline includes the active substance cytisine which acts as a partial nicotinic acetylcholine receptor agonist with high affinity for the $\alpha 4\beta 2$ receptor subtype. It reduces withdrawal symptoms and the rewarding effects of smoking by competing with nicotine to activate these receptors.[29] Varenicline has been shown to be highly effective, increasing the odds of long-term smoking cessation three-fold compared with quit attempts not aided by pharmacotherapy.[30] In direct comparison, it also appears to be more effective than bupropion but, to date, not NRT.[30]

- The cost per additional quitter for varenicline is approximately £2,170.[31] The ICER of varenicline compared with no pharmacotherapy has been estimated at between £950[32] and £1,140[22] per QALY gained, varying as a function of various assumptions. It is very cost-effective compared with minimal advice[22] (see Figure 1). Varenicline has been shown to be more cost-effective than either NRT or bupropion in the UK[33] and elsewhere,[34,35] though estimates vary greatly due to different methodologies applied (see Figure 2). Prolonging treatment duration from 12 to 24 weeks has also been shown to be cost-effective, resulting in an ICER of £622 per QALY.[36] Varenicline is therefore endorsed as effective and cost-effective treatment for smoking cessation by NICE guidelines.[21]

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3. Cost effectiveness of combined pharmacotherapy

- Monotherapy has been shown to be effective. However, more than two thirds of smokers will have relapsed by one year.[15,24,30] The rationale for combined pharmacotherapy is that medication may have synergistic effects when therapies with different pharmacological targets (e.g. NRT and bupropion) or different pharmacological profiles (e.g. nicotine patch and nicotine gum) are combined.[37]

- The combination of different forms of NRT has been shown to increase abstinence rates compared with single NRT.[15,38] Evidence for the combination of NRT with bupropion is less equivocal, suggesting an increase in short-term but not long-term abstinence compared with monotherapy.[39] Whilst there is some evidence that the combination of varenicline with bupropion,[40] and less so with NRT,[41] may be beneficial, there is currently insufficient evidence to draw firm conclusions.

- The combination of NRT and bupropion is cost effective compared with minimal advice (ranging between £973 – £2,918 per QALY gained) and counselling alone (range £440 – £1,319).[18] Evidence of combining NRT, bupropion and counselling compared with bupropion and counselling alone is weaker, suggesting only a marginal or no additional benefit.[27] However, one piece of indirect analysis comparing combination NRT with single NRT found a benefit and suggests an incremental cost per quitter at long-term follow-up of between £2,500 and £6,825.[37] A similar result is obtained when comparing NRT and bupropion with single NRT alone (range £2,000 – £6,200).[27;37] Both values compare favourably with the cost per quitter of monotherapy added to counselling.

- Given the relatively low cost of pharmacotherapy and the enormous health benefits of stopping smoking, smoking cessation interventions are considered among the most cost-effective available in the health care sector.[42] Whilst there are no direct economic evaluations of combination therapy, it is likely that even the small but significant benefits gained from combination rather than monotherapy would be translated in cost-effective outcomes compared with other health interventions for the treatment of smoking-related diseases (see Figure 3).[6]

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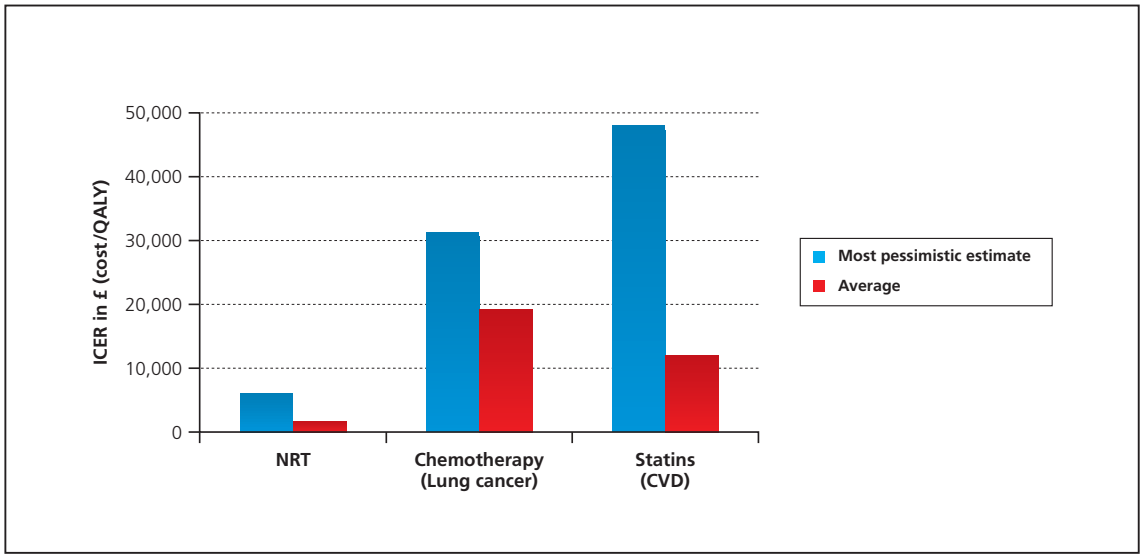
Figure 3: UK spend per QALY gained for treatments of smoking-related diseases in primary / secondary care compared with pharmacotherapy for smoking cessation.



Data from [10;18;43;44]

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