RESEARCH PAPER

Costs and benefits of smoking cessation aids: making a case for public reimbursement of nicotine replacement therapy in Australia

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Tobacco Control 2007;16:255–260. doi: 10.1136/tc.2006.017657

Background: Tobacco smoking is the leading preventable cause of morbidity and mortality in Australia and other developed countries. Of the pharmacological aids that are available for smoking cessation, bupropion (Zyban SR) is eligible for public reimbursement on the Australian Pharmaceutical Benefits Scheme (PBS), whereas nicotine replacement therapy (NRT) is not. Information on the cost-effectiveness and financial impact of public reimbursement of these strategies can better inform debate about their inclusion or exclusion in public reimbursement schemes.

Objective: To estimate the cost-effectiveness of bupropion and NRT, and the potential financial impact of public reimbursement of NRT in Australia.

Design: A cost-effectiveness analysis using a deterministic Markov model, and cost per disability-adjusted life year (DALY) averted over a lifetime as the outcome measure.

Population: Current smokers, motivated to quit, in Australia in 2000.

Interventions: (1) NRT; (2) bupropion; and (3) a combined strategy using bupropion as the first-line treatment and NRT in those who fail to quit smoking or have adverse reactions to bupropion.

Results: Quitting smoking can increase life expectancy of current smokers by 1–7.6 years depending on age at cessation and sex. Providing bupropion to current smokers who are motivated to quit would cost A\$7900 (95% uncertainty interval A\$6000 to A\$10 500) for each DALY averted; NRT patches would cost A\$17 000 (A\$9000 to A\$28 000) for each DALY averted, with similar results even if used as a second-line treatment following initial failure to quit using bupropion. If 6% of current smokers were to use NRT following inclusion on the PBS, this would result in an annual cost of A\$40–110 million to the PBS depending on the listed price.

Conclusions: Compared with other drugs included on the PBS, bupropion and NRT are both highly cost-effective smoking cessation interventions, and including NRT on the PBS would have a moderate financial impact. Given the sizeable health burden of smoking, and the large individual benefits of quitting smoking, increasing the availability of alternative aids and uptake of these strategies through public reimbursement would be a positive and rational step towards further reducing tobacco-related disease burden in Australia and other countries where NRT is currently not subsidised.

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Received 20 June 2006
Accepted 9 February 2007

Tobacco smoking is the largest preventable cause of morbidity and mortality in Australia and other developed countries. Despite projected declines in tobacco-related diseases in line with decreasing prevalence, tobacco is still expected to be among the leading causes of disease burden in 2016.¹ Worldwide, it is the second highest cause of death and fourth highest cause of disease burden.

Effective policies to control tobacco use are crucial. Although preventing individuals from starting smoking is an important aim of tobacco control, cessation in current smokers is also critical. As nicotine is highly addictive, smokers often require assistance to maintain abstinence. Modestly effective cessation aids are available, including pharmacological agents, such as bupropion (Zyban SR) and nicotine replacement therapy (NRT).^{2–3}

Australia has implemented many strong tobacco control policies. The retail price of tobacco in Australia is among the top three worldwide.⁴ Advertising and promoting tobacco products has been totally banned, pictorial pack warnings have recently been implemented, opportunities to smoke cigarettes in public places are severely limited and there is legislation in place forcing an upcoming ban of smoking in bars and hotels.^{5–7} Despite these measures, nearly one in five Australian adults still smoke daily, indicating the need for further strategies to encourage cessation.⁸

In 1995, the Australian government rejected a recommendation by the Pharmaceutical Benefits Advisory Committee to include NRT on the public reimbursement scheme—the Pharmaceutical Benefits Scheme (PBS).⁹ By contrast, bupropion was made available on the PBS in February 2001.¹⁰ The continued exclusion of NRT and inclusion of bupropion may or may not be a rational decision. Valid and comparable information on the cost-effectiveness and financial implications of including these interventions on the PBS are important inputs into this debate.

The cost-effectiveness of both NRT and bupropion has been studied previously.² A lack of consistency in the methods of these studies, however, makes comparisons difficult, and the context-specific nature of inputs into cost-effectiveness analyses such as disease outcomes means that these results may not be applicable to the Australian setting.^{2–11} This study aims to evaluate the cost-effectiveness of NRT and bupropion in the Australian context, as well as the potential financial impact of including NRT on the PBS.

Abbreviations: CPS-II, Cancer Prevention Study II; DALY, disability-adjusted life year; ICER, incremental cost-effectiveness ratio; NRT, nicotine replacement therapy; PBS, Pharmaceutical Benefits Scheme; SIR, smoking impact ratio

METHODS

We performed a cost-effectiveness analysis of NRT and bupropion for the prevention of tobacco-related diseases. The interventions modelled were treatment with NRT for a period of 6–12 weeks, or treatment with bupropion for a period of 7 weeks, as recommended by the treatment guidelines.¹² Transdermal patches were chosen as the delivery method for NRT because evidence suggests that all administration forms have similar efficacy,³ and patches have the lowest cost in Australia. We also considered the cost-effectiveness of using NRT as a second-line treatment when bupropion has not been successful. In this combined scenario, all those who failed to quit when given bupropion in the first year were given NRT in the second year of the model.

The target population for this analysis comprised current smokers who were motivated to quit, aged 20–79 years, in Australia in the year 2000. In 2000, there were 764 202 male and 553 727 female smokers in Australia. The cost perspective is that of the health system, including all government and patient contributions to drug costs and medical visits.¹³ Lifetime costs and benefits, modelled until death or age 100 years, were referenced to the year 2000, and evaluated using a discount rate of 3% per year.

The comparator for the intervention was “do nothing”, which would include the effects of mass-media campaigns and taxation on cigarettes, as these are currently widespread in Australia. As both the intervention and comparator groups will be exposed to the same scenario here, no costs have been included for the do-nothing scenario. The main outcome measure was the incremental cost-effectiveness ratio (ICER) of bupropion and NRT compared with the current practice scenario in year 2000, Australian dollars per disability-adjusted life year (DALY) averted. DALYs averted were equivalent to the number of healthy life years gained.

Model methods

We used Markov model techniques to predict the impact of cessation and continued smoking on smoking-related mortality in the future.¹⁴ Detailed methods are provided in a technical appendix; here we briefly describe the main methods. As exposure to tobacco affects a wide range of diseases, a mortality-based, rather than an incidence-based, approach was used to reduce complexity and increase transparency of the methods. Non-fatal health loss and the associated treatment costs were extrapolated for the relevant cause at the time of death, rather than at the time that they would have occurred, with discounting applied for the prior time period. The model operates in Microsoft Excel.

- T1: smoking cessation rate
- T2: mortality rate excluding smoking attributable mortality
- T3: mortality rate due to smoking in current smokers
- T4: mortality rate due to smoking in former smokers

Figure 1 Schematic diagram of the smoking cessation decision-analysis model.

Model structure

Three mutually exclusive states exist in the model—current smoker, former smoker and dead. At the end of each yearly cycle, portions of the cohort transit between the health states, using the possible transitions: “stay alive”, “die from a tobacco-related disease” or “die from a non-tobacco-related cause”. Those who remain alive either quit smoking or continue to smoke (fig 1).

Mortality from tobacco-related diseases

As there is no direct source of Australian cause-specific mortality stratified by smoking status, we first estimated smoking-related mortality for each cause in smokers and ex smokers combined. Lung cancer rates are estimated as the difference between Australian Bureau of Statistics age-specific and sex-specific lung cancer mortality, and lung cancer mortality from the American Cancer Society Cancer Prevention Study II (CPS-II)—the largest recent cohort study of exposure to tobacco and associated health outcomes.¹⁵ Because of the long lag between exposure and the incidence of other cancers and chronic obstructive pulmonary disease, it is not appropriate to use the current prevalence of smoking to determine the proportion of these causes of death caused by tobacco smoking. For these conditions, we calculated the smoking impact ratio (SIR): an artificial compound prevalence measure of accumulated past exposure to cigarette smoking in a population, derived from Australian lung cancer rates and those of smokers and non-smokers in CPS-II using the methods described by Peto.¹⁶ The SIR substitutes current prevalence in the usual population attributable fraction calculation.¹⁷ For all other conditions, the prevalence of smoking 1 year before the baseline year was used, assuming a short lag between exposure and outcomes.¹⁸

Reversal of tobacco-related disease risk

As the SIR includes accumulated risk from past as well as current exposure, we used information on time since cessation in former smokers from the Australian Diabetes, Obesity and Lifestyle Study¹⁹ along with the CPS-II estimates of risk reversal after smoking cessation,²⁰ to apportion smoking-attributable mortality between current and former smokers. Thus, for each former smoker in the Australian Diabetes, Obesity and Lifestyle Study, and for each tobacco-related disease, we calculated by how much their risk was reduced relative to that of a current smoker. By adding the total of these relative-risk values across all ex-smokers and taking this sum as a ratio over the combined risk in current and ex smokers, it gave us the proportion of total tobacco-related mortality for that age, sex and cause in ex smokers. For current smokers who had quit in the baseline year of 2000, either with or without the use of the interventions evaluated here, the same risk-reversal values were applied to the cause-specific tobacco-attributable mortality over time.

Excess mortality and adjustments for disability

The sum of excess mortality from all tobacco-related causes and non-smoker risk of mortality from all causes determines the risk of death at each age in the Markov model. This allows for the calculation of years lived by the cohort. The number of life years lived by the cohort is then adjusted for the probability of age-related, severity-weighted disability that is not attributable to tobacco. The latter was determined from the Australian Burden of Disease Study.²¹ To account for disability attributable to tobacco-related causes, a ratio of prevalent years lived with disability to death for each cause in the year 2000 was used as an average population estimate of smoking-related disability proportionate to each death.²¹

Table 1 Model uncertainty assumptions

Parameter	Uncertainty	Type of distribution	Source
OR of quitting—NRT	1.73 (1.62 to 1.85)	Triangular	Silagy, <i>et al</i> ¹⁰
OR of quitting—bupropion	2.54 (1.9 to 3.41)	Triangular	Woolacott, <i>et al</i> ⁶
Background quit rate	8.6% (7.9% to 9.3%)	Triangular	Silagy, <i>et al</i> ¹⁰
Intervention costs—NRT	A\$490 (A\$220–890)	Triangular	Own survey; variation in treatment length and strength
Intervention costs—patient contribution to bupropion	A\$36–96	Uniform	Variation in patient contributions
Relapse after initial cessation	10–48%	Uniform	Mikkelsen <i>et al</i> , Blondal <i>et al</i> , Daughton <i>et al</i> and Yudkin <i>et al</i> ^{22–25}

NRT, nicotine replacement therapy.

Intervention effectiveness

A meta-analysis of bupropion containing five trials estimated a pooled odds ratio (OR) of 2.06 (95% CI 1.77 to 2.40) for quitting at 1 year after intervention.² The OR for cessation 1 year after intervention calculated in a Cochrane review of 103 trials of transdermal NRT patches was 1.77 (95% CI 1.81 to 2.02).³ Using the quit rate of 8.6% (95% CIs 7.9% to 9.3%) in the placebo group from the meta-analysis of NRT patches³ as the “natural quit rate” that would be seen in the absence of interventions, we applied the OR for quitting from the meta-analysis to this natural quit rate to determine the quit rate under different intervention scenarios. The natural quit rate from the placebo group could be used in future years to indicate those quitting in the absence of intervention. In the combined scenario, we assume that the same OR applies to smokers who initially fail to quit with bupropion.

Evidence suggests that a relapse to smoking after initial abstinence occurs beyond 1 year. Smoking relapse rates following NRT treatment were calculated from the results presented in NRT trials with a long-term follow-up of 2–6 years. A relapse between 10% and 48% occurs up to 4 years after cessation.^{22–25} The range of these relapse rates are applied to the OR using the following formula:

$$OR = 1 + ((OR - 1) \times (1 - \text{relapse}))$$

Although no evidence exists on relapse for bupropion, we assumed that relapse occurs at the same rate as NRT. As we have no evidence regarding relapse in those who quit without a cessation aid, we have not applied relapse to the natural quit rate.

Intervention costs

The intervention costs for NRT patches were modelled for a 6–12-week treatment period, using 9 weeks as the midpoint, as used in many published trials and as recommended by Australian guidelines.¹² NRT is not listed on the PBS for general

patients, and thus users incur all costs. Costs for the treatment period, arising from our own survey of six pharmacies in Melbourne in 2002, ranged from A\$220 to A\$890, with a midpoint of A\$533, depending on length of treatment and strength of patch. This was included as a one-off cost in the first year in the intervention scenario.

The scheduled fee (ie, the government payment through the PBS) of a 7-week course of bupropion for the year 2000 was A\$238.95.¹² According to current PBS guidelines, this can be prescribed only once per year, and hence was included as a one-off treatment cost in the first year. As bupropion requires a prescription, the cost of a general practitioner's visit is also included, giving a total government contribution of A\$280. Patient contributions to both the prescription cost and the doctor's visit were derived from data provided by the Commonwealth government, giving a total cost of bupropion ranging from \$316 to \$376.

Cost offsets

Treatment costs, by age, sex and disease, were derived from the Australian Institute of Health and Welfare Disease Costs and Impacts Studies 2000–1 update.²⁶ As with the extrapolation of tobacco-related disability, a ratio of total health system costs to the number of deaths for each tobacco-related disease was applied at the time of death.

Financial cost of including NRT on the PBS

The financial cost of including NRT on the PBS was estimated based on prescription rates of NRT and bupropion among current smokers in the UK. In the UK, prescription rates rose from 0% of current smokers in 1999 to 8% (95% CI 6% to 10%) in 2002, a time period covering the introduction of subsidisation for both NRT and bupropion.²⁷ Other studies from the UK, since funding of NRT and bupropion was introduced, indicate that three times as many smokers have used NRT than bupropion.²⁸ To estimate the annual financial impact of including NRT on the PBS, we assumed that the total uptake of prescription NRT or bupropion would be 8%, as in the UK. We conducted a sensitivity analysis by estimating financial impact at higher levels of uptake (10%, 12%, 16% and 20%). For each scenario, we assumed that there is a three times greater preference for NRT over bupropion—that is, 2% would use bupropion and 6% would use NRT in the 8% uptake scenario. Users were assumed to purchase a full course of the treatment, and costs of the full course were determined as described above.

Uncertainty analysis

The impact of uncertainty around input values on the main outcome measures was estimated by Monte-Carlo simulation (1000 iterations) using @RISK (Palisade, Newfield, New York, USA; table 1).

Table 2 Years of life gained due to quitting smoking by age at the time of quitting and sex

Age group (years)	Male	Female
20–24	7.1	7.6
25–29	7.1	7.5
30–34	7.0	7.5
35–39	6.9	7.4
40–44	6.6	7.3
45–49	6.2	7.0
50–54	5.7	6.6
55–59	4.9	6.0
60–64	4.0	5.1
65–69	3.1	4.1
70–74	2.0	3.0
75–79	1.0	1.5

Undiscounted results presented.

Table 3 Costs, effects and cost effectiveness of smoking cessation interventions per 1000 smokers motivated to quit

	NRT	Bupropion
Number of additional quitters in first year	100	130
Number of additional quitters over the lifetime	14	18
Health gain (DALYs saved)	57	74
Cost of intervention (millions)	A\$1.1	A\$0.69
Potential cost savings due to reduced treatment of tobacco-attributable diseases	77000	100000
Cost effectiveness (A\$ per DALY saved)	17000 (9000 to 28000)	7900 (6000 to 10000)

DALY, disability-adjusted life year; NRT, nicotine replacement therapy.

All estimates rounded to two significant figures. Costs and health gain discounted at 3% per annum. Cost-effectiveness ratios are compared to "do nothing". Ranges are 95% uncertainty intervals.

RESULTS

The substantially increased mortality in current smokers translates into large gains in life expectancy from quitting smoking even when taking into account the lag period between quitting and a reduction in disease risk (table 2).

The initial cost of either NRT or bupropion is therefore offset by substantial health benefits from gains in length and quality of life as well as future cost savings from a reduced need to treat tobacco-related diseases (table 3). Bupropion, with an ICER of A\$7900 (95% uncertainty intervals A\$6000 to A\$11 000) per DALY averted is more cost effective than NRT, at A\$17 000 (95% uncertainty interval A\$9000 to A\$28 000) per DALY averted. Cost-effectiveness was the same when using NRT as a second-line treatment for those who fail to quit smoking using bupropion.

Annual cost of including NRT on the PBS and number of additional quitters

On the basis of a total uptake of prescription medicines for aiding smoking cessation in 8% of current smokers (6% using NRT and 2% bupropion), the annual financial cost would be between A\$40 and A\$110 million for NRT, depending on the final listed price and the treatment period, and A\$11 million for bupropion (table 4). The number of quitters as a result of prescription of cessation aids would be 2721 compared with the estimated 1600 because of current use of bupropion (4% of current smokers).²⁹ The financial cost of NRT to the PBS could be as high as A\$272 million in the unlikely event that the final listed price is A\$890 for a full course and that 20% smokers used prescription NRT.

DISCUSSION

Despite a high initial cost of both interventions, and a small increase in the total number of quitters, the large potential health gain for each individual smoker from cessation means that both NRT, bupropion alone and the combined scenario are

highly cost effective in the Australian setting, in line with the findings in the UK and New Zealand. All three have ICERs well below A\$42 000 per quality-adjusted life year—the threshold below which the Pharmaceutical Benefits Advisory Committee is unlikely to reject a drug.³⁰ Each of these interventions also has a cost per DALY less than Australia's gross domestic product per capita, which was A\$33 000 in 2000–1²⁶—the international standard for highly cost-effective interventions.²⁸ Both NRT and bupropion are also more cost-effective than other medicines included in the PBS that are primarily focused on prevention, such as statins for lowering cholesterol.³¹

These results support the continued listing of bupropion and additional listing of NRT for smoking cessation on the PBS. Improving the range of cessation aids that are reimbursed would better allow for individual preferences to be catered to and increase the uptake. In the UK, since funding of NRT and bupropion was introduced, three times as many smokers have used NRT than bupropion, indicating a clear preference for NRT.²⁸ General practitioners in Australia also indicate that NRT is the preferred strategy, and that there is a disincentive for its use because of high out-of-pocket costs to smokers in comparison with bupropion.³² Less financial burden on the quitter may also increase the number that completes the full course of treatment and, in turn, increase cessation rates. Besides the UK, there are also examples from other countries; NRT is currently subsidised in New Zealand, and is being trialled at subsidised rates in parts of the US.³³

The Australian government's argument for the exclusion of NRT in 1995 centred around the prohibitive financial burden to the PBS, given the high retail cost of NRT and the many smokers who would be eligible. In this analysis, we estimated the annual financial cost of NRT to the PBS to be A\$4073 million based on an estimated uptake rate of prescription NRT in 6% of current smokers, with 2% continuing to use bupropion. Although this is above the A\$10 million threshold that requires ministerial approval for listing of medicines on the PBS, it is

Table 4 Annual cost to the Pharmaceutical Benefits Scheme, and number of additional quitters, of including nicotine replacement therapy

	Percentage of current smokers using prescription medicine for aiding smoking cessation				
	4 (current)	8	12	16	20
Smokers using prescription NRT (%)	0	6	9	12	15
Smokers using prescription bupropion (%)	4	2	3	4	5
Annual financial cost to PBS of prescription NRT (millions of A\$)*—	—	40–110	69–166	79–220	98–272
Annual cost of prescription bupropion (millions of A\$)	22	11	16	22	27
Number of additional quitters owing to prescription NRT	—	1900 (1500–2200)	2800 (2300–3400)	3800 (3000–4500)	4700 (3800–5600)
Number of additional quitters owing to prescription bupropion	1600 (1400–1900)	820 (680–970)	1200 (1000–1500)	1600 (1350–1900)	2100 (1700–2400)

NRT, nicotine replacement therapy; —, not applicable.

All estimates rounded to two significant figures.

*Range reflects listed price and treatment length of NRT (A\$220–A\$890 per course).

small compared with, for example, the A\$1.1 billion that is spent on lipid-lowering agents each year.³³ Crucially, sales patterns of NRT in the UK also suggest that there was no change in over-the-counter sales, but only an increase in prescription sales.³⁴ This counters arguments that public reimbursement of NRT would simply shift costs from smokers to the government.

Several approaches could reduce this financial impact. One approach to reduce the financial burden to the PBS is price negotiation between the government and manufacturers. The cost of a course of NRT in Greece is as little as A\$83,³⁵ a fraction of the price used in this analysis. Given that listing on the PBS would increase the volume of sales, negotiating with manufacturers could result in a substantially lower NRT price. All NRT formulations (patch, gum and nasal sprays) could also be priced as a class; there is precedence for this—for example, in the case of statin drugs.³⁴ Reductions in price through any of these measures would also have a proportional positive effect in improving the cost-effectiveness. Another proposal is to fund NRT through a small increase in excise tax on cigarettes. Novotny *et al*³⁶ calculated that a 10% increase in excise tax on cigarettes in Australia would enable 25% of smokers to access NRT for 3 months.

There may be grounds other than financial ones that justify the continued exclusion of NRT from the PBS. One example is the belief that smokers should be responsible for their own cessation as they have chosen to smoke. However, many people requiring treatment for other conditions—for example, statin drugs for high cholesterol, have contributed to their own condition and have not been made to pay for their treatment.³⁷ Although information on cost-effectiveness or financial impact should never be used formulaically by decision makers, we believe that this analysis makes a strong case by demonstrating the lost opportunity to improve population health that is being forgone by the continued exclusion of NRT from the PBS.

Interventions such as legislation and enforcement of smoking bans in public places and comprehensive advertising bans are highly cost effective across all regions of the world.³⁸ Advocates rightly argue that the focus should be on these public control measures; however, many of these interventions are already in place in Australia and other countries, or legislated to come into effect soon. It is in these settings that the focus must be on cessation aids if progress is to be made towards reducing the health and economic burden of tobacco-related disease. It is important to note, however, that although both the interventions evaluated here are very cost effective, the number of lifetime quitters is not greatly increased. This highlights the need for the development of new cessation aids, such as a nicotine vaccine.³⁹

We have attempted to use the best evidence available in conducting this analysis, but as with any cost-effective analysis there are several limitations. The model used is based on mortality and requires extrapolation of non-fatal health outcomes, associating an average amount of morbidity with each event of death. However, as the non-fatal health outcomes are the dominant component of the healthy life measurements, this is unlikely to have a major effect. Potential health benefits arising from a reduction in environmental tobacco smoke have not been modelled. These are difficult to calculate given the lack of conclusive quantitative evidence on the excess risk involved in exposure, and an inability to measure the reduction in exposure caused by the small amount of cessation modelled. Finally, the same OR for quitting has been used in those using NRT as a second-line treatment as that calculated for NRT alone. This may have modestly overestimated the number of quitters and cost-effectiveness in the combined scenario.

What this paper adds

- It has long been known that tobacco smoking is one of the leading preventable risk factors for morbidity and mortality in much of the developed world.
- Given the addictive nature of nicotine smoking, cessation is difficult. Aids for smoking cessation are available; however, subsidisation varies between countries.
- Australia is at the forefront of tobacco control policy. Despite this, there is still a large scope for further reductions in tobacco-related morbidity and mortality if cessation can be encouraged.
- Individual cessation interventions are cost effective, even after population-wide strategies, such as smoking bans and raising tax on cigarettes, are implemented.
- Subsidisation of cessation interventions would encourage more smokers to quit, and lead to great reductions in mortality and morbidity in those who successfully quit smoking.

CONCLUSION

The benefits of quitting smoking as emphasised here are enormous. As a result, measures to increase the availability and range of smoking cessation aids and encourage uptake, such as public reimbursement, are highly cost-effective strategies. Public reimbursement of both NRT and bupropion in settings such as Australia would be a positive and rational move to reduce the health and economic burden of tobacco use.

ACKNOWLEDGEMENTS

We acknowledge that the analysis of AusDIAB datasets was completed within the ACE-Heart Disease project at Monash University. We thank Wayne Hall for his advice on policy implications of the analysis.

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Funding: NHMRC-Health Services Research Grant—Assessing Cost-Effectiveness (ACE)-Prevention Project, Centre for Burden of Disease and Cost-Effectiveness, School of Population Health, The University of Queensland, Herston, Queensland, Australia.

Competing interests: None declared.

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The Lighter Side

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