SECTION V ECONOMIC CONSIDERATIONS

10. COST-EFFECTIVENESS

10.1 ECONOMIC BURDEN OF LUNG CANCER IN AUSTRALIA

In 1996 lung cancer was the second most common malignant cancer in males and fourth most common in females[1]. Surgical resection provides curative therapy for early stage cancer, with five-year survival rates for early stage non-small cell lung cancer (NSCLC) ranging from 25%–67%. However, less than 20% of lung cancers are diagnosed when the cancer is still localized[2] and there are limited options for treatment of disseminated lung cancer. These factors have resulted in lung cancer being the most common cause of cancer death in males and the second most common in females[1]. In NSW the five year relative survival rates for lung cancer was the lowest of any cancer, at 10% for males and 12% for females, between 1980 and 1995[3].

The estimated burden of disease attributable to lung cancer in Australia is outlined in Table 1–10. Years of Life Lost (YLL) due to lung cancer are considerably higher than Years Lost due to Disability (YLD). This reflects the fact that the 'burden of cancer is dominated by mortality rather than lengthy periods of disability'[4].

Table 1–10 Burden of disease attributable to lung cancer in Australia, 1996[4]

	Total		Males		Females	
	Number	Per cent	Number	Per cent	Number	Per cent
Deaths	7 307	5.7	5 090	7.5	2 217	3.6
YLL	83 146	6.1	55 030	7.3	28 117	4.7
YLD	7 375	0.6	4 970	0.1	2 405	0.5
DALY	90 522	3.6	60 000	4.5	30 521	2.6

Abbreviations: YLL = Years of Life lost; YLD = Years Lost Due to Disability;
DALY = Disability Adjusted Life Year

The Australian Institute of Health and Welfare have estimated the costs of lung cancer at a macro level. In 1993–94 lung cancer was estimated to account for 5.6% of total health care system costs in Australia. It ranked fifth in terms of the most 'expensive' cancers in Australia with total health care expenditure on lung cancer estimated at $107 million in 1993–94 (this estimate includes hospital, medical, pharmaceuticals, nursing home and allied health services, public health programs, research, other institutional and non-institutional and administration expenditure[4]). Lung cancer ranks as the third most costly cancer for males aged 45–64 and the fourth most costly cancer for males and females aged over 65[4]. Total treatment costs for per case of lung cancer were estimated at $14 298 in 1993–94, which ranks twelfth in terms of the most costly cancer to treat[5]. However, there is relatively little micro-level information available in Australia about treatment patterns and resource use for lung cancer, particularly in terms of resource use by stage at diagnosis.

10.2 ROLE OF ECONOMIC EVIDENCE IN THE DEVELOPMENT OF GUIDELINES

The NHMRC has identified two main areas where economic evidence is important in the development of clinical practice guidelines:

- determination of which treatment alternatives are the most cost-effective
- determination of whether a proposed clinical practice guideline is cost-effective.

In the development of these guidelines, the emphasis has been in the first instance on identifying those interventions for which there is evidence of effectiveness, before addressing questions of cost-effectiveness. There is limited evidence available within Australia to assess the costs and cost-effectiveness of alternatives for management of lung cancer. However, there is a range of international literature that provides information about the relative cost-effectiveness of alternatives, and this information can be used to inform the development of these guidelines.

The approach taken in reviewing the economic evidence involved:

- identifying those areas where economic evidence is likely to be important
- identifying those areas where economic evaluation evidence is available
- reviewing and summarising the economic evaluation literature.

However, it is important to note that international economic evaluation literature is limited in its relevance to Australia because of differences in cost structures and reimbursement arrangements, and because the comparator in international studies may not reflect current practice in Australia.

A search was conducted using the databases Medline and Embase, covering the period 1993–2002. Economic evaluation literature that pre-dates 1993 was considered to be of limited relevance because of changes in technology, cost structures and management practices. The key words included lung cancer, economic evaluation, cost-effectiveness analysis, cost benefit analysis, cost analysis and cost. Articles were included if they were economic evaluations, that is, if they involved comparison of alternative interventions in terms of costs and consequences. A supplementary search was undertaken to identify economic evaluations of smoking cessation interventions. Articles were classified into seven main areas:

- smoking cessation and prevention
- screening
- initial assessment and follow-up
- lung cancer imaging including the use of PET
- treatment of non-small cell lung cancer (NSCLC)
- treatment of small cell lung cancer (SCLC)
- radon exposure (environmental exposure)(see Appendix 5).

These groupings reflected the main areas in which economic evaluation of interventions have been undertaken.

Articles were reviewed using the criteria recommended in the *How to compare the costs and benefits: evaluation of the economic evidence*[6]. The shadow price criteria in this document were used as a basis for assessing the relative cost-effectiveness of interventions. That is,

- interventions that fall below the threshold of $30 000 per life-year saved (LYS) are considered to be relatively cost-effective (good value for money) and can be recommended
- interventions that exceed a threshold of $100 000 per LYS are considered not to be cost-effective and cannot be recommended without a strong justification
- interventions that fall between $30 000 per LYS and $100 000 per LYS require further consideration.

However, assessment of overseas economic evaluations and even some Australian economic evaluations in these terms should be treated with some caution. Whether these costs and outcomes would be realised if the intervention were adopted in the Australian context depends upon a number of factors, but particularly on whether the comparator for the study reflects current practice in Australia.

Cost-effectiveness results from studies are presented as reported in the relevant studies (that is, in the currency and time period as reported in the study), but also, for comparative purposes, converted to 2001 Australian dollars. Results in terms of 2001 Australian dollars are reported in parentheses. The conversion was undertaken using the OECD purchasing power parity estimates (http:/www.oecd.org/std/ppp/) for the relevant year of the study to convert to Australian dollars for that year, then using the Australian Bureau of Statistics Health Price Index (weighted average of eight capital cities; ABS, 2002; Consumer Price Index Catalogue 6401.0) to convert the relevant costs to 2001 Australian dollars. Results in terms of 2001 Australian dollars are reported in parentheses below. However, in comparing across studies it should be noted that the results from different studies are not directly comparable. In particular, the scope of the studies may differ in terms of the range of costs and consequences considered, the perspective of the study and the choice of comparator. In addition, particularly for earlier studies, there may be important changes in cost structures and technology that limit comparability. The indicative cost-effectiveness estimates in 2001 Australian dollars should be treated as providing a guide to the likely cost-effectiveness of the interventions in the Australian setting, given the shadow prices suggested above.

The findings of the literature review are summarised below.

SMOKING CESSATION AND PREVENTION

A number of studies have been undertaken to assess the cost-effectiveness of various smoking cessation interventions, including:

- nicotine replacement therapy and other pharmacological therapies
- information programs and 'Quit smoking' campaigns delivered through various avenues (e.g. GP, pharmacist, community, media)
- counselling programs (e.g. group therapy and individual therapy)
- intervention on hospital admission.

In general cost-effectiveness studies of smoking cessation do not directly assess the potential impacts on lung cancer morbidity and mortality, and many studies report results in terms of intermediate outcome measures such as additional quitters. This is partly because of the number of additional assumptions required to extrapolate from additional quitters/non-smokers to impact on morbidity and mortality. However, given the importance of smoking as a risk factor for lung cancer, it is valuable to consider the cost-effectiveness of interventions aimed at reducing or preventing smoking.

In general, the cost-effectiveness research undertaken on smoking cessation and prevention indicates that smoking interventions represent good value for money. These results are primarily because of the relatively high level of benefits generated from the potential to avert years of life lost through reductions in morbidity and mortality, as well as because many of the interventions are relatively low cost compared with other health care interventions. Cost-effectiveness results do vary considerably between interventions. However, it is difficult to directly compare cost-effectiveness estimates across studies as estimates reflect not only the costs and effects of the alternative therapies but also different assumptions concerning the range of costs and benefits that are included in the evaluation.

INTERVENTIONS PROVIDED BY HEALTH CARE PROFESSIONALS

Smoking interventions can be delivered through a number of health care professionals including general practitioners, nurses, pharmacists and counsellors. There has been little cost-effectiveness research on this issue. Buck, Richmond et al[7] evaluated the cost-effectiveness of a GP delivered smoking cessation intervention known as Smokescreen, which involves GP training. The cost-effectiveness of this intervention was estimated at $183 (A$208) per additional abstainer. Viney, Haas et al[8] compared a number of different strategies including a GP based brief advice intervention and a more structured intervention consisting of a number of sessions. The brief advice approach was found to be more cost-effective at $6–$41 per quitter ($A7–$50).

Two studies have evaluated the cost-effectiveness of pharmacist intervention to assist smoking cessation. Cost-effectiveness estimates range from £300 (A$672) per one additional quit for pharmacists who were trained to provide 'more appropriate' information to people looking to stop smoking[9] to £509.60 (A$1051) for a program which consisted of a 'contract' between the pharmacist and patient and a series of counselling sessions over a 6 month period[10].

Counsellors provide another avenue through which smoking interventions can be delivered. The Mayo Clinic Nicotine Dependence Center (USA) provides a counselling service, which consists of an initial consultation and the formulation of an individual treatment plan, which may include group therapy, inpatient program and/or pharmacologic therapy. Croghan, Offord et al[11] evaluated this program and estimated a net cost per life-year gained of $6828 (A$11 693). Prathiba, Tjeder et al[12] evaluated the cost-effectiveness of a counselling programme provided to hospital in-patients and out-patients. They estimated the cost per life-year saved from such a program at £340–£426 (A$667–$836), and the cost of an additional quit was valued at £851 (A$1671).

These results indicate that appropriately trained health care professionals may be able to provide a cost-effective method through which to disseminate information on smoking cessation and/or conduct 'quit smoking' campaigns. However, more evidence is needed to make a recommendation.

GENERIC AND PERSONALISED SELF-HELP MATERIAL

One study, by Lennox, Osman et al[13], was found to have looked at the cost-effectiveness of generic versus tailored self-help material. This study evaluated the impact of computer tailored and non-tailored smoking cessation letters and found that the tailored letter did not increase cessation rates over and above that of the non-tailored letter. However, it was found to be effective in promoting a shift towards smoking cessation. The cost-effectiveness of the non-tailored letter (compared to no letter) was valued at £37 (A$49) per quitter, with the cost per life-year gained valued £50–£122 (A$67–$163). This study suggests that letter writing (either tailored or not tailored) is a cost-effective method of getting patients to quit smoking. However, non-tailored letter writing appears to be more cost-effective than tailored letter writing.

NICOTINE REPLACEMENT THERAPY (NRT)

Four studies were found which evaluated the cost-effectiveness of nicotine patches and one study evaluated the cost-effectiveness of Nicorette nasal spray. In all studies the incremental cost-effectiveness of nicotine patch or spray therapy was compared with (some form of) counselling alone. As outcome measures varied from study to study, the results have been set out in Table 2–10 (overleaf).

In all studies nicotine replacement therapy, when used as an adjunct to counselling, was found to be a cost-effective intervention. Therefore, there appears to be support for recommending the use of nicotine replacement therapy in combination with counselling services.

MASS MEDIA AND OTHER ANTI-SMOKING CAMPAIGNS

Anti-smoking campaigns and media campaigns have taken many forms including mass media campaigns, community programs and work-site smoking cessation programs. Cost-effectiveness studies have been undertaken to evaluate a handful of these campaigns.

Relative to other programs mass media campaigns appear to be relatively cost-effective. However, there is insufficient evidence to recommend one 'type' of campaign over another.

Table 2–10 Summary of NRT cost-effectiveness literature

Study	Study country	Comparator	Unit of benefit
Akehurst and Piercy 1994[14]	UK	GP counselling alone versus GP counselling and nicotine patch therapy	Cost-effectiveness per quitter is £3 074 (A$8 264) Marginal cost per quitter was £1 252 (A$3 365), marginal cost per death avoided £58 894 (A$158 336) and marginal cost per life-year gained £4 526 (A$12 341).
Akehurst and Piercy 1994[15]	UK	GP counselling alone versus GP counselling and nicotine nasal spray	Cost per life-year saved £1430 (A$3 844).
Fiscella and Franks 1996[16]	USA	GP counselling alone versus GP counselling and nicotine patch therapy	Cost of 1 additional lifetime quitter $7 332 (A$10 745) Incremental cost-effectiveness ranged $4 930–$10 043 (A$7 225–$14 718) per QALY for males and $4 955–$6 983 (A$7 262–$10 234) per female.
Stapleton, Lowin et al 1999[17]	UK	GP counselling alone versus GP counselling and nicotine patch therapy	Incremental cost per life-year saved range £395–£785 (A$775–$1 541).

Table 2–10 Summary of NRT cost-effectiveness literature *(continued)*

Study	Study country	Comparator	Unit of benefit
Wasley, McNagny et al 1997[18]	USA	Counselling alone versus GP counselling and nicotine patch therapy	Average cost per life-year saved: $965–$1 585 (A$1 414–$2 322) for males; $1 634–$2 360 (A$2 394–$3 459) for females Incremental cost per life-year saved: $1 796–$2 949 (A$2 632–$4 322) for males; $3040–$4 391 (A$4 455–$6 435) for females

Table 3–10 Summary of mass media and other anti-smoking campaigns cost-effectiveness literature

Study	Study country	Intervention type	Outcome
Mudde and De Vries 1999[19]	Netherlands	Mass media	US$12 per quit (A$17).
Ratcliffe, Cairns et al 1997[20]	Scotland	Mass media	£168–£369 per quit (A$330–$724).
Tillgren, Rosen et al 1993[21]	Sweden	Quit and win contest	US$188–$1 222 (A$342–$2 223) per life-year saved.
Stevens, Thorogood et al 2002[22]	UK	Targeted campaign for 'high-risk group' (Turkish speaking groups in London)	£105 (A$231) per life-year saved. Estimates ranged £33–£391 (A$73–$861).
Tengs, Osgood et al 2001[23]	USA	National school based education program	$4 900–$340 000 (A$6 826–$473 656) per quality adjusted life-year.
Warner, Smith et al 1996[24]	USA	Firm health promotion program	$894 (A$1310) per life-year saved. Estimates ranged $500–$2300 (A$733–$3370).
Viney, Haas et al 1996[8]	Australia	Mass media	$11–30 per quitter ($A13–36)

INTERVENTION FOR HOSPITALISED PATIENTS

Two studies were found which attempted to evaluate the cost-effectiveness of a hospital based smoking cessation interventions. Meenan, Stevens et al[25] estimated that the incremental cost per incremental quit at $3697 (A$5975) and the incremental discounted life-year saved ranged between $1691 (A$2733) and $7444 (A$12 031). This study provides some evidence that smoking cessation interventions for hospital in-patients may be cost-effective. However, more evidence is required.

OTHER PHARMACOLOGICAL THERAPIES INCLUDING BUPROPION

Nielsen and Fiore[26] conducted a cost benefit analysis of bupropion, nicotine transdermal patch (NTP) and a combination of the two therapies. This study found that bupropion alone, with a net benefit estimated at $338 (A$428), had a greater net benefit than either NTP at $26 (A$33), combination therapy at $178 (A$226) or placebo at $258 (A$327). Johnson, Lucas et al[27] also compared the cost-effectiveness of NTP against bupropion SR, and found that, despite similar effectiveness levels, bupropion SR was more cost-effective than NTP. The cost-effectiveness of bupropion hydrochloride as part of a health plan and work-site smoking cessation program was also evaluated and estimated to have a cost-benefit ratio of $1:4.10–$4.69 (A$1.30:5.33–6.09)[28].

These studies indicate that bupropion is a cost-effective intervention for smoking cessation and may be more cost-effective than nicotine replacement therapy. However, the number of studies is limited.

SCREENING

The prevailing consensus appears to be that mass screening programs to detect lung cancer are of doubtful cost-effectiveness. This is largely driven by relatively low rates of detection accuracy of plain chest x-rays. Estimates of cost-effectiveness for mass screening with plain chest x-rays vary from $9000 (A$11 414) per undiscounted life-year gained[29] to $93 000 (A$120 834)[30] per life saved. These estimates would appear to provide some support for mass screening. The former study assumes an 18% reduction in mortality, based on extrapolation of staging data from four randomised controlled trials, and assuming a 100% participation rate in annual screening of male smokers aged 45–80. However, the assumption of an 18% reduction in mortality is not adequately supported, given that trials on which the evidence was based did not show a mortality benefit. A further limitation is that consequences are not discounted. The latter study is a decision analytic model, with the detection rate based on results from a mass screening program in Japan. Both studies depend on the assumptions about detection rates, and the impact of early detection on survival.

The paucity of recent studies and the continued debate about whether plain x-rays are sensitive enough to detect lung cancer at a stage early enough to undertake curative treatment means that there does not appear to be strong support for recommending mass screening programs with plain x-rays on the basis of cost-effectiveness evidence.

Recent technological advances, primarily the development of CT screening, have led to improvements in the sensitivity of screening. Marshall, Simpson[31,32] and Okamoto[33] have evaluated the cost-effectiveness of CT screening for lung cancer. Marshall, Simpson[32]developed a decision analytic model to examine the cost-effectiveness of annual lung cancer screening based on CT for a high-risk cohort aged 60–74, combining data from the ELCAP project and the SEER registry. The model assumes that screening will shift the stage distribution at diagnosis. Based on this the cost per life-year saved is $19 000 ($A26 500), but in sensitivity analysis, this varied to $60 000 ($A85 000) per LYS. The same authors have used similar data to examine the cost-effectiveness of one-time screening and have estimated that the cost per life-year saved ranges from $5940 ($A8275) for a very high-risk cohort (lung cancer prevalence of 2.7%) to $23 100 ($A32 200) per life-year saved for a lower risk population of smokers. Okamoto[33] used a decision analytic model to examine the cost-effectiveness of CT screening compared with the current x-ray based screening in Japan, and concluded that while CT screening would be more expensive, it would also be more effective.

Despite the fact that CT screening is more expensive than screening by plain x-rays, the preliminary evidence suggests that the improvements in detection provided by CT scanning may outweigh the additional costs, leading to better estimates of cost-effectiveness for lung cancer screening. A major limitation of these studies is that the impact on mortality is based on extrapolation from screening results to a survival benefit. However, at this stage survival benefits from screening have not been demonstrated. Therefore, these cost-effectiveness estimates should be viewed with some caution as they are based on limited data on the effectiveness of CT screening, and may change with further evidence from randomised controlled trials. In general, the studies indicate that improvements in scanning technology that lead to better diagnostic accuracy (without parallel increases in cost) will improve the cost effectiveness of screening programs. For all screening programs, plain x-ray and CT, cost-effectiveness is significantly improved when screening is targeted at high-risk groups.

Table 4–10 Summary of screening cost-effectiveness literature

Study	Study country	Screening type	Unit of Benefit
Baba, Takahashi et al 1998[30]	Japan	Plain x-ray	Cost of a life saved ~$93 000 (A$117 942).
Caro, Klittich et al 2000[29]	USA	X-ray	Cost-effectiveness of $9 000 (A$11 413) per undiscounted life-year gained or less than $20 000 (A$25 364) per discounted life-year gained.
Chirikos et al 2002[34]	USA	CT scan	Incremental cost per life-year ratio $33 557 (A$45 789)–$90 022 (A$122 835).
Marshall, Simpson 2001[32]	USA	CT scan	High-risk cohort cost ~$19 000 (A$26 469) per life-year saved. ($10 800–$62 000 [A$15 045–$86 372])
Marshall, Simpson 2001[31]	USA	CT scan	High-risk cohort one time screen is $5 940 (A$8 275) per life-year saved. General population $23 100 (A$32 180) per life-year saved.

INITIAL ASSESSMENT AND FOLLOW-UP

There have been relatively few papers assessing the economic evidence for approaches to initial assessment of patients with suspected lung cancer. Raab, Hornberger et al[35] evaluated the cost-effectiveness of sputum cytology, when used as the first test preceding all other tests, in the diagnosis of lung cancer. Testing sputum cytology was found to be the dominant strategy as it lowered both medical costs and mortality risk. This study indicates that sputum cytology may provide a cost-effective option in the diagnosis of lung cancer. However, recommendations cannot be based on the findings on only one study. Therefore, this study can be taken as indicative of potential cost savings with further research required.

The Canadian Lung Oncology Group[36] have investigated the costs and outcomes of investigation for mediastinal disease for patients with apparently operable lung cancer, comparing mediastinoscopy with CT. They concluded that CT is likely to produce the same number or fewer unnecessary thoracotomies, and be less costly.

In a more recent study, the Canadian Lung Oncology Group have also undertaken a randomised controlled trial and comparison of costs of a limited and a full investigation strategy prior to the final decision regarding surgery. In the limited strategy patients underwent CT of the chest and mediastinoscopy, and proceeded to thoracotomy if there was no evidence of major mediastinal disease on CT, mediastinoscopy or both. In the full investigation strategy, patients also underwent bone scintigraphy and CT of the chest, liver, adrenal glands and head after mediastinoscopy. Patients in the full investigation group were less likely to have a thoracotomy, but there was no significant difference in the relative risk of thoracotomy without cure between the two strategies. While the full investigation strategy had higher costs associated with professional fees, overall, the average cost of full investigation was lower than for the limited strategy, because of costs of hospital episodes avoided. However, the difference in costs was not significant[37].

USE OF POSITRON EMISSION TOMOGRAPHY IN STAGING OF NSCLC

A number of studies have used decision analytic models to evaluate the cost-effectiveness of the use of Positron Emission Tomography (PET), in general FDG-PET, in staging and management of NSCLC. PET has been considered as both an adjunct and an alternative to conventional staging, which in most studies is assumed to be CT scanning. Most studies provide preliminary evidence to suggest that PET may be relatively cost-effective because of the potential to avoid unnecessary surgery through more accurate staging, and particularly through detection of disseminated disease. For example, Valk, Pounds et al[38] and von Schulthess, Steinert et al[39] both took a cost-minimisation approach and estimated that PET would be cost-saving as an adjunct or an alternative to conventional staging involving CT. However, neither study examines the impact on mortality, particularly the potential for PET to result in surgery avoided for potentially curable patients.

Dietlein, Weber et al[40] and Scott, Shepherd et al[41] examined the relative cost-effectiveness of a number of different potential strategies for incorporating PET in staging of NSCLC. Dietlein, Weber et al[40] concluded that PET was likely to be cost-effective (143 EUR/LYS) for patients with normal sized mediastinal lymph nodes when used as an adjunct to conventional staging. The results of Scott, Shepherd et al[41], suggest that PET is less cost-effective, but may be good value for money under some strategies, particularly for patients who had no mediastinal lymph node involvement on CT.

These results suggest that the cost-effectiveness of PET depends on how it is used in relation to conventional staging, and on the accuracy of the initial staging. The limitation of all the current cost-effectiveness analyses of PET is that they rely on estimates of sensitivity and specificity of PET based on relatively small case series rather than randomised controlled trials. Further, the relative cost-effectiveness of PET depends critically on the management decision made based on the PET results (that is, whether thoracotomy will be avoided, or whether the patient will have other treatment such as chemotherapy, as an addition or alternative to thoracotomy)[42]. Thus, it is important to assess the cost-effectiveness of PET in the local context and using evidence from randomised controlled trials. Two recent studies provide new evidence that will be critical in determining the value of PET in management of NSCLC. van Tineren, Hoekstra et al[43] have undertaken a randomised controlled trial of pre-operative assessment of patients with suspected Stage I-III NSCLC. Their results suggest that PET may avoid thoracotomy in 20% of patients. Although they have not as yet reported cost-effectiveness analysis, these results suggest that PET may be relatively cost-effective. However, preliminary cost-effectiveness results from another randomised controlled trial and cost-effectiveness analysis[44] suggest that PET may not be cost-effective in management of Stage I–II NSCLC.

TREATMENT OF NON-SMALL CELL LUNG CANCER (NSCLC)

There is relatively limited information about the cost-effectiveness of the range of treatments for non-small cell lung cancer, including the value of surgery for potentially operable disease, the appropriateness of adjuvant therapy and the appropriate choice of chemotherapy agent for disseminated cancer.

FOLLOW UP AFTER SURGICAL MANAGEMENT

There is very little information on cost-effectiveness of alternative follow-up strategies. Younes, Gross et al[45] compared the cost-effectiveness of a strict follow-up regime (consisting of strict visits, imaging and laboratory examinations) with infrequent visits. The study found that, for patients with resected NSCLC, the strict follow-up strategy was more expensive but did not lead to a significant difference in interval between recurrence.

Gilbert, Reid et al[46] evaluated whether follow-up by a thoracic surgeon after cancer resection, as opposed to a GP, altered survival. The cost per recurrence detected by a thoracic surgeon was $4367 (A$5108) compared with $1105 (A$1293) for the cost per recurrence detected by a GP. No 5-year survival benefit for surgeon-detected recurrences was found. Therefore, follow-up via a GP was found to be relatively cost-effective.

Similarly, Egermann, Jaeggi et al[47] examined the costs and outcomes of a strict protocol of regular follow-up for 10 years including clinic visits and chest radiography following resection for NSCLC, although it is not clear whether the comparator was no follow-up or a less frequent protocol. They concluded that the costs per life-year saved from the strict protocol were high.

CHEMOTHERAPY FOR ADVANCED (STAGE IIIB AND IV) NSCLC

A number of studies evaluating different chemotherapy regimes for advanced NSCLC have been undertaken since 1995, although there is considerable overlap between studies in terms of the modelling approaches used and the trial and other data used to estimate effectiveness. The results are summarised in Table 5–10.

In general, these studies, particularly the review studies, provide evidence that chemotherapy provides a small survival and quality of life gain that is relatively cost-effective compared with supportive care[48]. The majority of these studies provide evidence to suggest that the incremental cost-effectiveness of some chemotherapy regimes is less than $A30 000 per life-year gained, although cost-effectiveness estimates vary considerably. However, there is insufficient evidence at this stage to recommend one particular chemotherapy agent or regime over others on the basis of cost-effectiveness. However, it should be noted that these results are sensitive to the method of estimating or extrapolating survival and quality of life data from trials, to the chemotherapy regimes, to the relative costs of different chemotherapy regimes, and to the method of delivery of chemotherapy, with inpatient care being more costly than outpatient care. While the studies provide evidence to suggest that some chemotherapy regimes appear to be relatively more cost-effective than others, and in some instances cost-saving, extrapolating these results to the Australian context is not appropriate, as the relative cost-effectiveness is largely driven by the relative costs of the different chemotherapy regimes and modes of delivery, which can vary internationally.

Table 5–10 Results of studies investigating costs and outcomes of alternative chemotherapy regimens

Studies	Study country	Study questions	Conclusions
Palmer and Brandt 1996[49]	Italy	Comparison of 4 cisplatin regimens: G+P; MIP; E+P; NVB+P	No significant difference in survival Based on $/tumour response, gemcitabine & cisplatin is more cost-effective
Will, Berthelot et al 2001 Berthelot, Will et al [51]	Canada†	Comparisons of a range of chemotherapy regimes with best supportive care (BSC) including VLB+P; NVB; NVB+P; PAX+P (3 doses); G	VLB+P dominates BSC Incremental cost of chemotherapy compared with BSC ranges from $1 900–$27 000/LYS ($A2 353–33 447); $2 658–$37 841/QALY ($A3 300–$46 300) At a threshold of $A30 000/QALY, preferred regime is NVB+P; for lower thresholds VLB+P is preferred, for higher, G is preferred; Results vary if outcome measure is LYS
Koch, Johnson et al 1995[52]	Germany	Comparison of gemcitabine versus ifosfamide/etoposide; assumes equal efficacy	Gemcitabine has the potential to be cost saving
Billingham et al 2002[53]	UK	Comparison of MIC chemotherapy plus standard care versus palliative care alone.	Chemotherapy more costly than palliative care. Incremental cost-effectiveness ratio of £14 620 (A$31 333) per life-year gained.
Clegg, Scott et al 2002[48]	UK	Comparison of a range of chemotherapy regimens with BSC: G; G+P; NVB; NVB+P; PAX; PAX+P– various doses; DOC; DOC 2nd line Based on a review of 33 clinical trials and construction of a costing model	Incremental cost compared with BSC varied from £4 091 ($A8 633) for NVB to £46 610 ($A98 360) for PAX. At a threshold of $A30 000/LYS NVB; NVB+P; G; G+P; and PAX+P cost-effective

Table 5–10 Results of studies investigating costs and outcomes of alternative chemotherapy regimens *(continued)*

Studies	Study country	Study questions	Conclusions
Annemans, Giaccone et al 1999[54]	The Netherlands, Belgium, Spain and France	Comparison of paclitaxel & cisplatin versus teniposide & cisplatin for advanced NSCLC	Trial results show no difference in survival or quality of life PAX+P more expensive but additional responders Not clear that all costs were considered
Smith, Hillner et al 1995[55] Hillner and Smith 1996[56]; 1998[57]	USA	Comparison of three chemotherapy regimes: NVB; NVB+P; VIN+P	Incremental $/LYS ranged from $15 500 (NVB+P versus VIN+P)—$22 100 (VIN+P versus NVB alone) ($A23 000–$33 000)
Evans and Le Chevalier 1996[58] Evans 1998[59]	Canada†	Comparison of chemotherapy regimes with BSC: NVB alone, NVP+P; VIN+P; VP-16-P; VLB+P	NVB alone; NVB+P (delivered in outpatient setting); VLB+P and VP-16-P are dominant. Cost per LYS for other therapies less than $A20 000
Evans 1996[60], 1997[61]	Canada†	Comparison of gemcitabine with BSC Incremental $/LYS	Incremental $/LYS $630–$16 230 depending on assumptions and numbers of cycles ($A854–$22 007)
Earle and Evans 1999[62]	Canada†	Comparison of PAC+P with standard E+P for advanced NSCLC	Incremental $/LYS $76 370–$138 578 based on trial protocol ($A84 451–$153 242) Outpatient protocol incremental $/LYS 30 619 ($A33 000)

Table 5–10 Results of studies investigating costs and outcomes of alternative chemotherapy regimens *(continued)*

Studies	Study country	Study questions	Conclusions
Leighl, Shepherd et al 2002[63]	Canada	Comparison of 2nd line docetaxel with BSC based on the TAX 317 trial	Incremental $/LYS ranged from $31 776–$57 749 ($A37 168–67 548), but results were sensitive to changes in survival estimates, increasing to $117 434 ($A137 362)
Sacristan, Kennedy-Martin 2002[64]	Spain	Comparison of G+P with E+P	No differences in survival were found; Gem+P was lower cost and had higher response rate and longer time to progress. Preferred on a cost-minimisation basis
Ramsey, Moinpour et al 2002[65]	USA	Comparison of NVP+P with PAX+P	No difference in survival or cancer related quality of life; NVB+P less costly; preferred on a cost-minimisation basis
Earle and Evans 1997[66]	Canada†	Comparison of PAC alone with BSC	Incremental Cost per LYS varied from $4 778–$21 377 depending on assumptions ($A6 428–$28 986)
Rubio-Terres, Tisaire et al 2002[67]	Spain	Comparison of DOC+P; PAX+P; PAX+C	No difference in survival Doc+P less costly; preferred on cost-minimisation basis

†POHEM is a population health micro-simulation model developed by Statistics Canada, which is used to evaluate interventions. The lung cancer model was developed in collaboration with oncologists at the Ottawa Regional Cancer Centre (ORCC).

Abbreviations: BSC: best supportive care; DOC: docetaxel; DOC+P: docetaxel & cisplatin; E+P: etoposide & cisplatin ; G: gemcitabine; G+P: gemcitabine & cisplatin; MIC: ; MIP: mitomycin, ifosfamide & cisplatin; NVB: vinorelbine; NVB +P: vinorelbine & cisplatin; NVP+P: ; PAX: paclitaxel; PAX+C: paclitaxel & carboplatin; PAX+P: paclitaxel & cisplatin ; T+P: teniposide & cisplatin ; VIN+P: vindesine & cisplatin; VLB+P: vinblastine & cisplatin; VP-16-P

RADIOTHERAPY AND COMBINATION THERAPIES

Coy, Schaafsma et al[68] has estimated the incremental cost per LYS and cost per QALY for high dose palliative radiotherapy for advanced NSCLC compared with BSC to be $12 253 per LYS ($A13 500) and $17 012 per QALY ($A18 900). However, this study was not based on trial data and the results were sensitive to assumptions about cost and survival benefit.

Evans, Will et al[69] have used the Canadian POHEM model to examine the cost-effectiveness of combined modality interventions (pre and post operative chemotherapy and pre and post operative chemotherapy and radiotherapy) for Stage III NSCLC. They estimate that the cost per LYS ranges from $3 348–$14 958 ($A4 500–20 300) for Stages IIIA and IIIB cancer, and may be lower with outpatient therapy. However, again, these results are not based on trial data and are sensitive to estimates of cost and survival gain.

TREATMENT OF SMALL CELL LUNG CANCER (SCLC)

The cost-effectiveness literature with regards to the treatment of small cell lung cancer is sparse, with only 5 articles located. Four studies evaluated alternative chemotherapy options including: pre emptive administration of G-CSF for patients treated with conventional myelosuppressive cytotoxic chemotherapy, routine use of granulocyte colony stimulating factor, cisplatin in combination with either etoposide or etoposide phosphate, and oral versus intravenous etoposide. A further study on the effectiveness of prophylactic cranial irradiation was also reviewed.

As each study tackles a different treatment question it is difficult to draw conclusions or make any recommendations from the available literature. At best, these studies provide an initial indication of possible cost-effectiveness for certain treatment options.

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