Pergamon

European Journal of Cancer Vol. 32A, No. 13, pp. 2249–2255, 1996

Printed in Great Britain
0959-8049/96 $15.00 + 0.00

PII: S0959-8049(96)00298-5

Original Paper

The Cost-effectiveness of Navelbine Alone or in Combination with Cisplatin in Comparison to Other Chemotherapy Regimens and Best Supportive Care in Stage IV Non-small Cell Lung Cancer

W.K. Evans[1] and T. Le Chevalier[2]

[1]University of Ottawa and Ottawa Regional Cancer Centre, Ontario Cancer Treatment and Research Foundation, 501 Smyth Road Ottawa, Ontario, Canada K1H 8L6; and [2]Institut Gustave-Roussy, Villejuif, France

An economic evaluation was undertaken, using data from European and Canadian randomised controlled trials of chemotherapy in advanced non-small cell lung cancer (NSCLC), to determine the cost and cost-effectiveness of single-agent vinorelbine (Navelbine, NVB) therapy and NVB in combination with cisplatin (NVB-P) compared to vindesine in combination with cisplatin (VDS-P), standard regimens including VP-16-cisplatin (VP-16-P) and vinblastine-cisplatin (VLB-P) and best supportive care (BSC). The Population Health Model (POHEM) developed by Statistics Canada was used to model the cost of care per patient, the total burden of cost to the Canadian healthcare system and the cost-effectiveness of the therapeutic interventions relative to BSC and to standard chemotherapy regimens, expressed as the cost per life year gained (LYG). Based on this analysis, VLB-P proved to be the most cost-effective chemotherapy regimen relative to BSC, as it increased average survival by 0.27 years while reducing costs by $3265 per case. NVB-P increased survival to a greater degree (0.44 years/patient) while inpatient administration increased costs by $2451 per case, for a cost-effectiveness ratio of $5551 per LYG. Outpatient administration, which reduced the cost of care per case by $473, was shown in the model to be the most cost-effective way to administer this regimen. Relative to VP-16-P and VLB-P, outpatient NVB-P regimen proved to be cost-effective at $7902 and $16 404 per LYG, respectively. Based on our estimates, a variety of chemotherapy regimens, including outpatient NVB-P, are cost-effective in the management of advanced (Stage IV) NSCLC and competitive with some commonly used healthcare interventions. Therefore, cost and cost-effectiveness should not be barriers to the utilisation of NVB-P therapy in Canada.

Key words: navelbine, cisplatin, chemotherapy, lung cancer, cost

Eur J Cancer, Vol. 32A, No. 13, pp. 2249–2255, 1996

INTRODUCTION

THE HEALTH Protection Branch of Health Canada recently approved the use of vinorelbine (Navelbine, NVB) for the treatment of advanced non-small cell lung cancr (NSCLC). This approval was based, in part, on the results of a large European clinical trial which showed that the treatment of advanced NSCLC with NVB, a semisynthetic vinca alkaloid, in combination with cisplatin (NVB-P) resulted in a higher response rate and a longer survival than vindesine plus cisplatin (VDS-P) ($P = 0.04$) or Navelbine (NVB) alone ($P = 0.01$) [1, 2]. Because of the perception that NVB represents a useful, but expensive new agent, it was felt that it would be useful to estimate the cost and cost-effectiveness of NVB-based regimens using a model of lung cancer man-

Correspondence to W.K. Evans.
Received 29 Feb. 1996; revised 29 Jul. 1996; accepted 29 Sep. 1996.

agement in Canada developed at Statistics Canada [3–5]. Also, it was felt that NVB ± P should be compared for cost-effectiveness with VDS-P and other standard chemotherapy regimens [VP-16-cisplatin (VP-16-P), and vinblastine-cisplatin (VLB-P)] and the policy of best supportive care (BSC). The economic analyses were undertaken using drug utilisation and survival data from the trial reported by Le Chevalier which compared NVB alone to NVB-P and VDS-P [1, 2] and a National Cancer Institute of Canada (NCIC) clinical trial (BR5) which compared VDS-P to best supportive care (BSC) [6].

MATERIALS AND METHODS

The lung cancer costing model

A Population Health Model (POHEM) is being developed by Statistics Canada to simulate the health of Canadians [3–5]. POHEM generates a synthetic cohort of people with the demographic characteristics, risk factor exposures and health histories typical of Canadians. The model includes data on diagnostic methods, treatment and its outcomes, healthcare utilisation and direct care costs. The perspective of the costing model is that of the government as payer in a universal healthcare system. The POHEM model provides a framework in which the impact of diagnostic and therapeutic options can be assessed. The lung cancer submodel assigns individuals according to the histological cell types and stage distribution observed in cases from the Canadian Cancer Registry in 1988.

Diagnostic evaluation

The simulated patients in the POHEM lung cancer submodel are assigned a standard set of diagnostic tests, procedures and visits, including an initial medical contact (family physician), a specialist consultation and diagnostic work-up appropriate for their disease stage. For Stage IV, the number of physician assessments and associated fees were determined from the number of chemotherapy treatments given and the expected number of physician encounters during these treatments. The cost of laboratory and imaging studies was estimated from their reported frequency in the methods sections of the study protocols and the fees listed in the Ontario Schedule of Benefits. It was assumed that tests were not duplicated and that treatment was uncomplicated.

Chemotherapy specific costs

The cost of chemotherapy and its administration was calculated from the dosage and administration schedules reported in detail for NVB, NVB-P and VDS-P in the European trial [1, 2]. The Stage IV patients in this trial were randomised to one of three regimens: (1) Navelbine alone at a dose of 30 mg/m^2 intravenously (i.v.) weekly; (2) Navelbine 30 mg/m^2 (i.v.) weekly plus cisplatin 120 mg/m^2 on day 1 and day 29, then every 6 weeks; or (3) vindesine 3 mg/m^2 weekly for 7 weeks; then every 2 weeks, plus cisplatin at the same dose and schedule as for NVB-P. Time spent by nursing and pharmacy personnel in the preparation and administration of NVB, NVB-P and VDS-P was determined using the Canadian Management Information System (MIS) for pharmacy workload and by measuring the time taken to administer NVB and NVB-P in the Chemotherapy Treatment Unit of the Ottawa Regional Cancer Centre (ORCC). The nursing and pharmacy personnel costs were determined by multiplying the amount of time expended by the hourly salary rate, including benefits, at the ORCC in 1993. Similarly, the costs associated with the administration of VP-16-P (VP-16 100 mg/m^2 i.v. days 1–3, cisplatin 25 mg/m^2 days 1–3 every 3 weeks) and VLB-P (VLB 5 mg/m^2 i.v. day 1 and 8 and cisplatin 100 mg/m^2 i.v. days 1 every 4 weeks) were determined. Chemotherapy and anti-emetic (ondansetron/dexamethasone) drug costs were based on their acquisition costs at the ORCC in 1993. Equipment and supplies to prepare and deliver the chemotherapy were quantified and costed by the pharmacy and nursing staff of the ORCC.

Hospitalisation and other costs

High-dose cisplatin was administered in hospital during the NCIC and Le Chevalier studies and it was assumed that each hospitalisation required 2 days. The daily cost of hospitalisation for chemotherapy was based on the actual cost of treating patients at the Princess Margaret Hospital as determined during a previous costing study [7], adjusted to 1993 costs by multiplying the 1984 cost by the increase in the average daily cost of operating tertiary health care facilities in Canada between 1984 and 1993 (increase of 12.4%). In addition, we estimated the cost of NVB-P administration using an outpatient schedule currently being used in a National Cancer Institute of Canada clinical trial (Navelbine 30 mg/m^2 weekly and cisplatin 50 mg/m^2 on days 1 and 8 every 4 weeks). The cost of radiotherapy, as well as the overhead costs of clinic visits (so-called hotel costs) were extracted from the same study [7] and adjusted to 1993 dollars by multiplying by the increase in the Consumer Price Index (41.1%).

Best supportive care and terminal care costs

The cost of managing Stage IV NSCLC with BSC was obtained from the economic analysis from the BR5 study [7] and adjusted to 1993 Canadian dollars ($(CND) = £2.1187 Sterling). The cost of terminal care for Stage IV chemotherapy-treated patients included similar cost elements; however, consistent with the BR5 study, patients received less palliative radiotherapy. In the present study, we assumed that chemotherapy-treated patients used fewer hospital bed days during terminal care (17.1 versus 23.6 days; $11 471 versus $15 831) and would receive less radiotherapy ($528 versus $745), as was observed in the BR5 trial.

Survival data

For this study, the survival data for all patients treated with NVB, NVB-P and VDS-P was obtained on computer diskette from the principal investigators of the European trial [1]. From these data, the survival curve for patients with Stage IV disease was extracted in order to compare it to that of the Stage IV patients treated with VDS-P and BSC in the NCIC BR5 trial [6]. The survival curves for the Stage IV patients treated with VDS-P in the two studies were superimposable (Figure 1). The survival of patients treated with VP-16-P and VLB-P was assumed to be the same as that of VDS-P, based on previous randomised trials [8, 9].

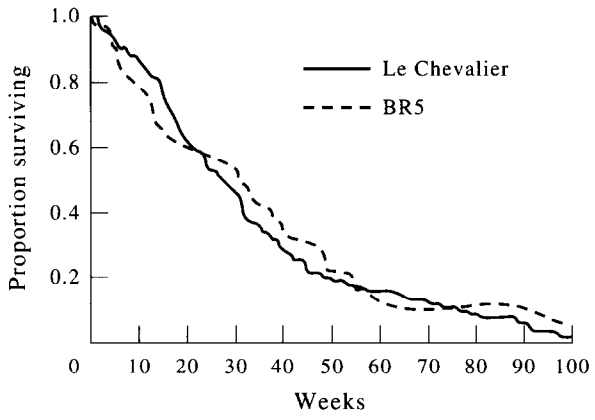

Figure 1. Survival of stage IV patients treated with VDS-P in the BR5 and Le Chevalier trials.

Cost and cost-effectiveness

The cost of treating an individual patient with each of the regimens and the impact of the various interventions on the cost of healthcare in Canada was determined in the microsimulation model assuming that all Stage IV lung cancer patients would be treated with chemotherapy. The cost-effectiveness of NVB, NVB-P, VDS-P and the other chemotherapy regimens was determined by dividing the total cost of care, including the diagnostic, treatment, follow-up, relapse and terminal care costs, by the estimated survival gain relative to BSC. A similar analysis was carried out using the 'standard' regimens of VLB-P and VP-16-P as the base case instead of BSC.

This study was commissioned after the results of the European trial were published. No restraints were placed on the principal investigator by the funding agency (Burroughs Wellcome Inc. Canada, Trans-Canada Road, Kirkland, Quebec). Funding was provided to the Ottawa Regional Cancer Centre which, in turn, contracted with Statistics Canada for use of the POHEM microsimulation software and the provision of analytic expertise for the economic analysis.

RESULTS

Cost per case

Table 1 summarises the estimated cost per case to manage a patient with Stage IV disease, including diagnosis, treatment, follow-up, relapse and terminal care, where treatment consists of NVB alone, inpatient and outpatient NVB-P, VDS-P, VP-16-P and VLB-P regimens or BSC. BSC was estimated to cost $27 348 per patient. Chemotherapy plus additional hospitalisation increases the cost per case for the inpatient NVB-P and VDS-P. An actual reduction in the total cost per case for VLB-P, VP-16-P, NVB alone and for outpatient NVB-P results from the decreased costs of terminal care hospitalisation when patients were treated with chemotherapy (17.1 hospital days with chemotherapy versus 23.6 days with BSC).

Total cost and cost-effectiveness

Table 2 shows the total direct care costs to the Canadian healthcare system for each treatment intervention, assuming that all 4411 new cases of Stage IV NSCLC diagnosed in Canada in 1988 were treated. Similar to the cost/case data, the POHEM model projects a notable net reduction in healthcare costs with the use of VLB-P, VP-16-P and NVB alone relative to BSC. These savings would amount to $14.4, 8.02 and 6.4 million, respectively. Outpatient NVB-P would decrease the cost of care by $2.09 million, while inpatient NVB-P and VDS-P would result in a net increase of $10.8 and 14.2 million, respectively. Alternatively, if outpatient NVB-P therapy were to replace the least expensive chemotherapy (VLB-P), there would be a net increase in the cost of care of $12.3 million.

Based on these cost estimates and the survival of patients in the Canadian and European trials, the cost-effectiveness of the various therapies was calculated relative to BSC and to the standard treatment regimens. Table 3 shows cost-effectiveness, expressed as the cost per life year gained, or, in the case where there is a reduction in costs relative to BSC, as the cost saving per case. The standard therapies of VLB-P and VP-16-P were the most cost-effective as both increased the average survival by 0.27 years, while decreasing the cost per case by $3265 and $1818, respectively. NVB alone increased survival relative to BSC, while saving $1447 per case. NVB-P (inpatient and outpatient) increased survival by an average of 0.44 years, but outpatient NVB-P

Table 1. Per case cost components of chemotherapy regimens and best supportive care (1933 $CDN)

	NVB alone	NVB-P (OUT-PT)	NVB-P (IN-PT)	VDS-P	VP-16-P	VLB-P	BSC
Diagnostic tests	785	785	785	785	785	785	785
Other tests	230	230	230	230	230	230	230
Hospitalisation	8356	8356	8356	8356	8356	8356	8356
Chemotherapy	3754	4827	7751	8410	3369	1922	NA
Follow-up*	759	759	759	759	759	759	**
Terminal care							
Palliative XRT	528	528	528	528	528	528	745
Hospitalisation	11 471	11 471	11 471	11 471	11 471	11 471	15 831
Clinic costs							1401
Total cost of care	25 883	26 956	29 880	30 539	25 498	24 051	27 348
Incremental cost	(1465)	(392)	2532	3191	(1850)	(3297)	NA

NVB, Navelbine; NVB-P, Navelbine-cisplatin; OUT-PT, outpatient; IN-PT, inpatient; VDS-P, vindesine-cisplatin; VP-16-P, VP-16-cisplatin; VLB-P, vinblastine-cisplatin; BSC, best supportive care; NA, not applicable. * Follow-up may extend beyond the first year. ** Follow-up costs incorporated in the clinic costs.

Table 2. Total cost of care components for chemotherapy regimens and best supportive care (n = 4411; 1993 CDN$/,000)

	NVB alone	NVB-P (OUT-PT)	NVB-P (IN-PT)	VDS-P	VP-16-P	VLB-P	BSC
Diagnosis	3463	3463	3463	3463	3463	3463	3463
Other tests	1015	1015	1015	1015	1015	1015	1015
Hospitalisation	36 858	36 858	36 858	36 858	36 858	36 858	36 858
Chemotherapy	16 559	21 292	34 189	37 097	14 861	8478	NA
Follow-up	3348	3348	3348	3348	3348	3348	NA
Terminal care	51 314	50 875	50 875	51 374	51 374	51 374	77 601
Total cost*	112 556	116 850	129 748	133 154	110 918	104 535	118 936

*The component costs shown are rounded figures to the nearest thousand, so real totals may differ from a summation of the figures.
NVB, Navelbine; NVB-P, Navelbine-cisplatin; OUT-PT, outpatient; IN-PT, inpatient; VDS-P, vindesine-cisplatin; VP-16-P, VP-16-cisplatin; VDS-P, vinblastine-cisplatin; BSC, best supportive care; NA, not applicable.

saved $473 per case while inpatient NVB-P increased the cost per case by $2451 for a cost-effectiveness of $5551/LYG relative to BSC. VDS-P was the least cost-effective treatment approach at $11 876 per LYG.

Sensitivity analysis for survival

As patients in the European trial [1, 2] may have been selected for good performance status and other favourable prognostic factors, their survival may have been better on this basis alone. However, sensitivity analyses show that NVB alone and outpatient NVB-P save money relative to BSC, even when the observed gain in survival is reduced by 50% (Table 4). Inpatient NVB-P does not save money relative to BSC, but would be considered cost-effective over the same range of survival reduction.

Sensitivity analysis for number of terminal hospital days

NVB, NVB-P, VP-16-P and VLB-P all appear to be cost-effective in the model relative to BSC, in part, because patients receiving chemotherapy are assigned fewer hospital days during terminal care, based on observations made in the NCIC BR5 study [6]. It seems reasonable to assume that chemotherapy regimens that cause a survival gain may also control cancer-related symptoms, thus resulting in less hospitalisation. Due to hospital bed closures in Canada, the length of hospital stay for patients with terminal lung cancer may have decreased since the BR study. Table 5 shows the cost-effectiveness or the cost saved per case for the NVB regimens, assuming a range of hospital bed stays for terminal care. Even if it is assumed that chemotherapy-treated patients have the same length of stay as BSC patients (23.6 days), the cost-effectiveness of NVB-P remains acceptable and, for outpatient administration, less than $8500/LYG.

Cost-effectiveness of NVB and NVB-P relative to standard chemotherapy

Table 6 summarises the cost effectiveness of NVB, NVB-P and VDS-P regimens compared to two of the standard treatments for Stage IV disease, VP-16-P and VLB-P. Outpatient NVB-P is cost-effective relative to VP-16-P ($7902/LYG). Inpatient NVB-P is less cost-effective at $25 082/LYG and NVB alone is least attractive in this comparison at $28 573/LYG. The low cost of VLB-P makes the cost-effectiveness of NVB-P (inpatient and outpatient) less attractive relative to VLB-P in this comparison, although outpatient NVB-P would generally still be considered cost-effective at $16 404/LYG.

DISCUSSION

The lung cancer costing model developed by Statistics Canada provides a useful framework in which to estimate the cost-effectiveness of new treatment interventions. The base case in the model for Stage IV NSCLC is best supportive care. This reflects the most common management approach for Stage IV NSCLC in Canada. Increasingly, however, it is recognised that chemotherapy has a small, but definite impact on the survival of patients with Stage IV NSCLC [10–12] and that it can improve cancer-related symptoms [13–16]. For these reasons, it is increasingly likely that chemotherapy will be used in the palliation of patients with advanced NSCLC. The availability of information on the cost and cost-effectiveness of the current chemotherapy options for the management of this disease will help to inform physicians who must make decisions concerning the treatment of these patients.

The results of the Le Chevalier trial suggest that NVB-P is superior to other commonly used chemotherapy approaches in the management of medically suitable lung cancer patients [1, 2]. However, NVB is a relatively expens-

Table 3. Cost and cost-effectiveness of chemotherapy regimens in comparison to BSC (n = 4411; 1993 $CDN)

	NVB alone	NVB-P (OUT-PT)	NVB-P (IN-PT)	VDS-P	VP-16-P	VLB-P	BSC
Average survival (years)	0.8756	1.0328	1.0328	0.8626	0.8626	0.8626	0.5912
Average years saved	0.2844	0.4416	0.4416	0.2714	0.2714	0.2714	NA
Total life years saved	1254	1948	1948	1197	1197	1197	NA
Cost saving per case	1447	473	NA	NA	1818	3265	NA
Cost per life year saved ($)	NA*	NA*	5551	11 876	NA*	NA*	NA

NVB, Navelbine; NVB-P, Navelbine-cisplatin; OUT-PT, outpatient; IN-PT, inpatient; VDS-P, vindesine-cisplatin; VP-16-P, VP-16-cisplatin; VLB-P, vinblastine-cisplatin; BSC, best supportive care; NA, not applicable. * These interventions have lower costs and greater survival, therefore cost-effectiveness is not displayed.

Table 4. Sensitivity analysis for cost-effectiveness of Navelbine assuming survival gain or −25% and −50% (n = 4411, 1993 $CDN)

	NVB OBS	NVB (−25%)	NVB (−50%)	NVB-P OBS (Out)	NVB-P (−25%) (Out)	NVB-P (−50%) (Out)	NVB-P OBS (In)	NVB-P (−25%) (In)	NVB-P (−50%) (In)
Average survival (years)	0.8756	0.7948	0.7151	1.0328	0.9245	0.8079	1.0328	0.9245	0.8079
Average years saved	0.2844	0.2036	0.1239	0.4416	0.3333	0.2167	0.4416	0.3333	0.2167
Cost per life year saved ($)	NA*	NA*	NA*	NA*	NA*	NA*	5551	7592	12022
Cost saved per case (versus BSC)	1447	1379	1336	473	394	319	††	††	††

NVB OBS, observed survival on Navelbine in the Le Chevalier study; NVB, Navelbine; NVB-P OBS, observed survival of Navelbine-cisplatin; NVB-P, Navelbine-cisplatin; OUT, outpatient; IN, inpatient; NA*, not applicable as these treatments are associated with increased survival relative to BSC and decreased cost. †† These treatments are associated with increased cost per case relative to BSC.

ive new agent and inpatient NVB-P will be seen by many as prohibitively expensive relative to the small survival gains associated with this approach.

Our analysis using the POHEM lung cancer model has clearly demonstrated that inpatient NVB-P is associated with increased costs relative to best supportive care, but is cost-effective as $5551/LYG. If all 4411 patients with Stage IV NSCLC diagnosed in 1988 were treated with inpatient NVB-P, total healthcare costs in Canada would increase by an estimated $10.8 million. Although this might appear to argue against the use of NVB-P, in reality, only a fraction of the total Stage IV NSCLC patients would ever be candidates for chemotherapy. Many patients with lung cancer are not medically appropriate for chemotherapy because of comorbid conditions and poor performance status.

Outpatient NVB-P would actually save $473 per case while increasing survival by an average of 0.44 years. If all 4411 patients were treated with outpatient NVB-P, there would actually be a net saving of $2.08 million to the Canadian healthcare system. Although NVB alone does not prolong survival relative to VDS-P, it is also an option to be considered when compared to BSC, as it has few toxicities and is less costly, saving $1447/life year gained. It may be of particular value in older, medically frail patients who insist on a trial of therapy.

Although chemotherapy is used relatively uncommonly in Canada in the treatment of Stage IV NSCLC, those patients who are treated, tend to be treated with either VP-16-P or VLB-P. Randomised studies have demonstrated equivalency between these regimens and VDS-P [8, 9] and both are easily administered and relatively inexpensive outpatient regimens. Assuming these trial results are correct, our analysis shows that VLB-P and VP-16-P are the most cost-effective regimens in the treatment of Stage IV NSCLC when compared to BSC. Because the model assumes that chemotherapy-treated patients use fewer hospital days for terminal case, the use of either of these standard regimens could potentially result in a reduction in overall healthcare costs. If all patients with Stage IV disease were treated with the VLB-P combination, there would be a saving of $3265/case or a net saving of up to $14.4 million to the healthcare system. For VP-16-P, the saving per case would be $1818 for a maximum potential saving to the healthcare system of $8.02 million.

In all the cost comparisons, VDS-P proved to be the least cost-effective regimen with a cost per life year saved of $11 876. Despite its demonstrated superiority in the Canadian NCIC trial, its toxicities and the difficulty of accessing hospital beds for the administration of high-dose cisplatin have largely curtailed the use of VDS-P in Canada [17].

A weakness in the POHEM costing model is that it does not account for the complications of treatment and their cost. In developing the lung cancer model, the general lack

Table 5. Sensitivity analysis for cost-effectiveness of Navelbine-based on number of terminal care hospital days

	Number of hospital days	Total terminal care costs ($ 000)	Total care costs ($ 000)	Cost per life year gained compared to BSC	Cost saved per case
NVB alone	14.1	42 708	103 950	NA*	3398
	17.1	51 314	112 556	NA*	1447
	18.1	54 183	115 425	NA*	796
	19.1	57 051	118 294	NA*	146
	23.6	69 691	131 203	9779	0††
NVB-P outpatient	14.1	42 342	108 318	NA*	2408
	17.1	50 875	116 850	NA*	473
	18.1	53 719	119 695	389	††
	19.1	56 564	122 539	1850	††
	23.6	69 363	135 338	8420	††
NVB-P inpatient	14.1	42 342	121 215	1170	††
	17.1	50 875	129 748	5551	††
	18.1	53 719	132 592	7011	††
	19.1	56 564	135 437	8471	††
	23.6	69 363	148 236	15 042	††

See Table 4 for symbol definitions.

Table 6. Cost and cost-effectiveness of Navelbine, Navelbine-cisplatin and vindesine-cisplatin relative to VP-16-cisplatin and vinblastine-cisplatin as standard therapies (n = 4411; 1993 $CDN)

	NVB alone	NVB-P (OUT-PT)	NVB-P (IN-PT)	VDS-P	VP-16-P	VLB-P
Chemotherapy costs ($, 000)	16 559	21 292	34 190	37 097	14 861	8478
Total care costs ($, 000)	112 556	116 850	129 748	133 154	110 918	104 535
Average years saved	0.0130	0.1702	0.1702	0	0	0
Cost per life year saved versus VP-16-P	28 573	7902	25 082	NCE	NA	NA*
Cost per life year saved versus VLB-P	139 881	16 404	33 584	NCE	NCE	NA

NVB, Navelbine; NVB-P, Navelbine-cisplatin; OUT-PT, outpatient; IN-PT, inpatient; VLB-P, vinblastine-cisplatin; VP-16-P, VP-16-cisplatin; VDS-P, vindesine-cisplatin; NA, not applicable; NA*, regimen produces similar survival at reduced cost by $1477/case; NCE, not cost-effective.

of information on the frequency of complications of therapy and the resources used in their management led us to simplify the model and to assume that all treatment and diagnostic procedures were uncomplicated. Although the frequency and severity of the chemotherapy toxicities are well described in the Le Chevalier manuscript, the lack of detail concerning the amount of hospitalisation required to manage these toxicities made it impossible to measure their costs. In a recent study by Smith and associates, of the cost-effectiveness of the Le Chevalier study in the American healthcare environment, the cost of toxicities was estimated to be only 5% of the total healthcare costs [18]. Therefore, the degree to which we may have underestimated the true costs of care is likely to be small.

We made the assumption in this analysis that the number of terminal care hospital days for chemotherapy-treated patients would be reduced from 23.6 days for best supportive care to 17.1 days [6]. This was the difference observed in the NCIC BR5 study in 1984, but may no longer be the case. In recent years, the average length of hospital stay has been reduced. It is possible that the length of stay for terminal care for advanced NSCLC may also have shortened. If, in fact, it has, the sensitivity analysis shows that combination chemotherapy is less cost-effective, but still well within the range regarded as cost-effective for a healthcare intervention in Canada [19] or the United States [20, 21].

Laupacis and associates have reported that new medical technologies that cost between $20 000 and $40 000 per quality adjusted life year (QALY) saved are acceptable to the Canadian public [19]. The cost-utility of all the chemotherapy regimens reviewed in the present report probably falls within or below the range described above. We did not undertake a cost-utility analysis because of the limited amount of quality of life data available on treated, advanced NSCLC patients [6, 21, 22].

When the cost-effectiveness analyses were performed with VP-16-P as standard treatment, outpatient NVB-P is cost-effective at $7902/LYG, whereas inpatient NVB-P and NVB alone are much less cost-effective at $25 082/LYG and $28 573/LYG, respectively. When VLB-P is used as the standard, NVB alone is not cost-effective at $139 881 per LYG, but the NVB-P in- and outpatient regimens are in the cost-effective range at $33 584 and $16 404 per life year gained, respectively. If NVB-P as outpatient therapy were to replace VLB-P as first-line therapy for Stage IV NSCLC, there is the potential to increase the total healthcare expenditure in Canada by $12.3 million, an increase of 11.8%, again assuming that all patients with Stage IV were treated with chemotherapy. In reality, the model greatly overestimates the impact of chemotherapy for NSCLC on the Canadian healthcare budget, as only a minority of patients are offered treatment. This may change as drugs such as Navelbine, which have a better therapeutic index, make it possible to offer a treatment with a modest survival benefit and less risk of toxicity to the patient.

A decision to treat a patient with Stage IV NSCLC is a complex one which must consider the patient's overall medical condition and performance status, the effectiveness of therapy, the quality of life of the patient on treatment and the patient's preferences. Although cost is one consideration, this analysis suggests that NVB-P is cost-effective relative to healthcare interventions that are generally considered acceptable to the Canadian population. Cost, therefore, should not, in and of itself, be a barrier to the use of NVB-P in the management of Stage IV NSCLC in Canada.

Acknowledgement—This study was made possible by a grant provided by Glaxo Wellcome, Inc.

DISCLAIMER

This analysis is based on Statistics Canada's Population Health Model (POHEM). The assumptions and calculations underlying the simulation results were prepared by Dr W.K. Evans and the responsiblity for the use and interpretation of these data is entirely that of the author.

1. Le Chevalier T, Brisgand D, Douillard JY, *et al.* Randomized study of vinorelbine and cisplatin versus vindesine and cisplatin versus vinorelbine alone in advanced non-small cell lung cancer: results of European multicenter trial including 612 patients. *J Clin Oncol* 1994, **12**, 360–367.
2. Le Chevalier T, Pujol JL, Douillard JY, *et al.* A three-arm trial of vinorelbine (Navelbine) plus cisplatin, vindesine plus cisplatin, and single-agent vinorelbine in the treatment of non-small cell lung cancer: an expanded analysis. *Semin Oncol* 1994, **21**(Suppl. 10), 28–34.
3. Evans WK, Will BP, Berthelot J-M, Wolfson MC. Diagnostic and therapeutic approaches to lung cancer in Canada and their costs. *Br J Cancer* 1995, **72**, 1270–1277.
4. Evans WK, Will BP, Berthelot J-M, Wolfson MC. Estimating the cost of lung cancer diagnosis and treatment in Canada: the POHEM model. *Can J Oncol* 1995, **5**, 408–419.
5. Wolfson MC. POHEM—A framework for understanding and modelling the health of human populations. Presented at Bureau of Census 1992 Annual Research Conference, Arlington Virginia. In *Proc Ann Res Conf* 1992, 261–282.
6. Rapp E, Pater JL, Willan A, *et al.* Chemotherapy can prolong survival in patients with advanced non-small-cell lung cancer—

report of a Canadian multicenter randomized trial. *J Clin Oncol* 1988, **6**, 633–641.
7. Jaakkimainen L, Goodwin PJ, Pater J, *et al.* Counting the costs of chemotherapy in a National Cancer Institute of Canada randomized trial in non-small-cell lung cancer. *J Clin Oncol* 1990, **8**, 1301–1309.
8. Dhingra HM, Valdivieso M, Carr DT, *et al.* Randomized trial of three combinations of cisplatin with vindesine and/or VP-16 in the treatment of advanced non-small cell lung cancer. *J Clin Oncol* 1985, **3**, 176–183.
9. Ruckdeschel JC, Finkelstein DM, Ettinger DS, *et al.* A randomized trial of the four most active regimens for metastatic non-small cell lung cancer. *J Clin Oncol* 1986, **4**, 14–22.
10. Grilli R, Oxman AD, Julian JA. Chemotherapy for advanced non-small cell lung cancer: how much benefit is enough? *J Clin Oncol* 1993, **11**, 1866–1872.
11. Souquet PJ, Chauvin F, Boissel JP, *et al.* Polychemotherapy in non-small cell lung cancer: a meta-analysis using updated individual patient data from 52 randomized clinical trials. *Lancet* 1993, **342**, 19–21.
12. Non-small Cell Lung Cancer Collaborative Group. Chemotherapy in non-small cell lung cancer: a meta-analysis using updated individual patient data from 52 clinical trials. *Br Med J* 1995, **311**, 899–909.
13. Osoba D, Rusthoven JJ, Turnbull KA, *et al.* Combination chemotherapy with bleomycin, etoposide and cisplatin in metastatic non-small cell lung cancer. *J Clin Oncol* 1985, **3**, 1478–1485.
14. Fernandez C, Rosell R, Abad-Esteve A, *et al.* Quality of life during chemotherapy in non-small cell lung cancer patients. *Acta Oncol* 1989, **28**, 129–133.
15. Ellis PA, Smith IE, Hardy JR, *et al.* Symptom relief with MVP (mitomycin C, vinblastine and cisplatin) chemotherapy in advanced non-small-cell lung cancer. *Br J Cancer* 1995, **71**, 366–370.
16. Kris MG, Gralla RJ, Potanovich LM, *et al.* Assessment of pretreatment symptoms and improvement after EDAM mitomycin vinblastine (EMV) in patients with inoperable non-small cell lung cancer (NSCLC). *Proc Am Soc Clin Oncol* 1990, **9**, 229, 883 (abstract).
17. Raby B, Pater J, MacKillop WJ. Does knowledge guide practice? Another look at the management of non-small cell lung cancer. *J Clin Oncol* 1995, **13**, 1904–1911.
18. Smith TJ, Hillner BE, Neighbours DM, *et al.* Economic evaluation of a randomized clinical trial comparing vinorelbine, vinorelbine plus cisplatin, and vindesine plus cisplatin for non-small cell lung cancer. *J Clin Oncol* 1995, **13**, 2166–2173.
19. Laupacis A, Feeney D, Detsky AS, Tugwell P. How attractive does a new technology have to be to warrant adoption and utilization? Tentative guidelines for using clinical and economic evaluations. *Can Med Assoc* 1992, **146**, 473–481.
20. Shulman KA, Lynn LA, Glick HA, Eisenberg JM. Cost-effectiveness of low-dose zidovudine therapy for asymptomatic patients with human immunodeficiency virus (HIV). *Ann Int Med* 1991, **114**, 798–802.
21. Tengs TO, Adams ME, Pliskin JS, *et al.* Five-hundred life-saving interventions and their cost-effectiveness. *Risk Analysis* 1995, **15**, 369–390.
22. Ganz PA, Figlin RA, Haskell CM, *et al.* Supportive care versus supportive care and combination chemotherapy in metastatic non-small cell lung cancer. Does chemotherapy make a difference? *Cancer* 1989, **63**, 1271–1278.
23. Feld R. Quality of life in patients with non-small cell lung cancer treated with chemotherapy. *Eur J Cancer Clin Oncol* 1987, **3**, 357–359.

Acknowledgements—The author acknowledges the extensive help and support of the Health Analysis and Modeling Group at Statistics Canada, including Jean-Marie Berthelot, B. Phyllis Will, Christian Houle and Ronna Egan. The author also wishes to thank the staff of the Ottawa Regional Cancer Centre who provided data on drug preparation and supply costs (D. Pollack) and nursing time and supplies (J. Stapleton and C. Burpee).