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OP1. THE RELEVANCE OF RESPONSE SHIFT IN PERCEPTION OF HEALTH FOR UTILITY EVALUATION

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Purpose: We previously developed a linear analogue self-assessment (LASA) scale anchored at "perfect health - worst health" (range: 0-100) for serial assessment of utility values in cancer clinical trials (Br J Cancer 77:985-91, 1998). This approach is based on the hypothesis that patients may change their perception of health over time. Within a colon cancer trial (SAKK 40/93; Ann Oncol 10:775-782, 1999), we examined whether patients undergoing surgery with or without adjuvant chemotherapy change the internal standard on which they base their subjective health estimation. **Methods:** After radical resection of adenocarcinoma of the colon (pT1-4 pN>0 M0 and pT3-4 pN0 M0) and perioperative chemotherapy, patients were randomized to 3 treatment arms: observation only (A), 5-FU 450 mg/m^2 plus Levamisol (B), or 5-FU 600 mg/m^2 (C). Patients estimated their pre-surgery health among other quality of life indicators both before surgery and retrospectively thereafter, and their pre-adjuvant health both at beginning of randomly assigned chemotherapy or observation and retrospectively about 2 months later. Thereafter, current subjective health was assessed. Paired t-tests were used to test the hypotheses of no change. **Results:** Patients' estimates of their pre-surgery health were worse after surgery than before (N=127, mean change=6.7, p=0.01), and their pre-adjuvant estimates were worse under treatment or observation than at the beginning (N=132, mean change=7.1, p=0.001), in agreement with other indicators. Chemotherapy had no impact on these changes attributed to a response-shift. Conventionally assessed changes between beginning of adjuvant treatment or observation and two months later indicated no change in subjective health (N=122, mean change=0.6, p=0.8). **Conclusions:** Patients with colon cancer substantially reframe their internal standard of health both under radical resection and under adjuvant chemotherapy or observation. This finding argues against the stability of utility estimates, which in cancer clinical trials is often assumed.

OP2. COST-EFFECT ANALYSIS USING MULTIVARIATE ANALYSIS OF VARIANCE.

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Economic data was collected in parallel with conventional clinical data, for a subgroup of 315 patients with non-small cell lung cancer, during a multi-centre, UK based, MRC sponsored, phase III trial randomizing between continuous hyperfractionated, accelerated radiotherapy (CHART) versus conventional radiotherapy. A detailed breakdown of medical, travel and community costs was recorded on an individual patient level for a period of one year. The standard TN-staging and histology of disease were recorded along with simple demographic information. The follow-up was until death, and hence survival time has been used as the measure of effect. The novel application of a well established statistical method, multivariate analysis of variance or MANOVA, has been applied. This enables the detection of general departures from a common mean location within the cost-effect plane between arbitrarily defined patient groups. It can incorporate the principle of incremental cost-effect analysis by allowing first for a deviation due to treatment and then testing for group deviations. It has an advantage over the cost-effect ratio by being able to distinguish, for example, between two equal ratios of 2000 £ per life-year where one ratio is due to a saving of £500 for a loss of ¼ life-year, and other is due to a cost of £20,000 for a gain of 10 life-years. The method is demonstrated by testing between four groups, artificially defined according to which quadrant the patient lies in, when the cost-effect plane undergoes a translation such that the mean is at the origin. When the groupings are chosen according to diagnostic factors, no significant differences were detected. The treatment did cause a significant difference due to the experimental arm being more expensive with improved survival compared to the conventional arm.

OP3. AN EXPLORATION OF ALTERNATIVE APPROACHES FOR ANALYSING INCOMPLETE COST DATA: THE CASE OF CHEMOTHERAPY VERSUS PALLIATIVE CARE IN ADVANCED NON-SMALL CELL LUNG CANCER

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Increasingly economic evaluations of health technologies are using patient-level data, most commonly in clinical trial settings. Missing data, for measures of both benefit and cost, often complicates analysis. The focus for this paper is the analysis of costs where some resource use data are missing. A number of alternative approaches are demonstrated, including: (1) complete case analysis, (2) regression-based imputation, (3) expectation-maximisation (EM) algorithm methods, and (4) Heckman selection models. The EM algorithm is an iterative maximum likelihood procedure. The Heckman procedure involves simultaneous estimation of two models: the regression equation of interest (i.e. the cost model) and a model to predict observations with missing data. Neither the EM algorithm nor Heckman models have been widely used in health economic evaluations.

The cost data reported here are from a randomised trial of chemotherapy versus standard palliative care in advanced non-small cell lung cancer ('MIC2'). A subset of 118 trial patients (58 on each arm) was selected for the cost study. Patterns of care from trial entry until death were recorded retrospectively. Complete resource use data were available on 82 (71%) patients. The complete case analysis found that patients on the chemotherapy arm experienced more hospital in-patient days (mean: 11.6 versus 6.9 days) but a similar number of outpatient attendances (mean: 5.6 versus 5.5 visits) and GP visits (mean: 12.3 versus 11.9). Patients on the standard palliative arm had more hospice in-patient days (3.8 versus 3.8 days) and hospice care team visits (2.1 versus 1.8 days).

However, this complete case analysis is inefficient and likely to be biased. The level of bias is explored in the paper through the presentation of a series of cost analyses using the alternative approaches to handling missing data. This has allowed the degree of consistency of results from alternative methods to be identified.

OP4. COST COMPARISON BETWEEN STEREOTACTIC CORE NEEDLE BIOPSY VERSUS SURGICAL EXCISION BIOPT IN THE NETHERLANDS.

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Yearly, approximately 7000 Dutch women with non-palpable breast lesions are referred for -histological examination by means of diagnostic surgical excision biopsy (EXB). Although this procedure is accurate, it is rather invasive, requires general anaesthesia, hospitalisation for 1 to 2 days and is costly. Also, even with negative test results patients should anticipate mutilation of the breast. Recently, less invasive alternatives such as stereotactic core needle biopsy (CNB) have emerged. This procedure can be performed in an outpatient setting and has potential for savings.
The present cost study is part of an ongoing study (COBRA) on the accuracy and cost-effectiveness of CNB as compared to EXB. A total of 970 women underwent CNB and in case no malignancy was found also underwent EXB. For the cost study data were collected prospectively in 5 Dutch hospitals. As stereotactic equipment is expensive, the costs of CNB depend on the extent of centralisation of this facility. The impact of economies of scale was assessed in four different scenarios varying from strictly centralised to decentralised.
The cost of EXB, including procedure, hospitalisation, pathologic examination and complications was 1150 Euro. In case CNB would be employed decentralised in all 114 hospitals, the average procedural costs were estimated to be 1068 Euro. If, however, availability of CNB would be restricted to 10 specialised breast clinics the cost per procedure reduced to 473 Euro. The patient cost (travel time and costs) were estimated at 13 Euro in a fully decentralised scenario versus 44 Euro in a centralised scenario.
Apparently, CNB is less costly, even though the extent of centralisation strongly affects the potential savings. In conclusion, we feel that core needle biopsy is a promising technique. Yet, the full economic evaluation of the COBRA-study should be awaited, which will provide insight in the balance between cost and effects of CNB.

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OP5. COST-UTILITY ANALYSIS OF THE ADJUVANT INTERFERON ALPHA 2-B TREATMENT IN MELANOMA.

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Melanoma's incidence is increasing in an alarming way. Though no curative treatment is available, Kirkwood et al. found a survival gain associated with the adjuvant treatment of interferon alpha 2-b (IFN). The high dose regimen recommended in this study rendered the treatment toxic and expensive. Economic analysis have been carried out but their results were based on gross estimations and failed to measure directly the costs of this treatment and its influence on the quality of life.

We carried out a cost-utility analysis of the IFN adjuvant treatment in melanoma. Eighteen patients (melanoma stage III) were followed in order to asses the resource consumption and consequently the costs related specifically to the IFN adjuvant treatment. Utility values were measured with the Time Trade-Off method by using a representative sample of the general population consisting of 108 respondents. The gain in survival was based on existing data.

We considered a third-party perspective. The costs associated with the IFN treatment state and the relapse state were respectively 46 080 $ CAN and 12 300$ CAN. We also assessed the costs related to the without symptoms state which decreased with time being 280 $ CAN the first two years, 130 $ CAN from the 3rd to 5th year and 90 $ CAN the following years. Median utility values of 0.58 and 0.08 were found respectively for the IFN treatment health state and the relapse health state. We hypothesized that a utility value of 1 and 0 were associated respectively to the without symptoms health state and death.

By considering a 35 year time horizon and a discounting rate of 4%, we obtained a cost-utility ratio (C/U) of 46 580$ CAN/QALY. The cost-effectiveness ratio (C/E) (excluding utility values) was of 33 000 $ CAN/saved life years. The elements to which the final results were sensitive were the unit cost of IFN, the administered doses of IFN, the utility value of the IFN treatment state and the discounting rate.

Though the C/U ratio found in this study is above the beneficial threshold ratio considered by Laupacis et al. and is less favorable than those found in previous economic analysis of this treatment, it does not render the adjuvant IFN treatment in melanoma unfavorable. With the C/U and C/E ratios found in this analysis, it will remain in the hands of decision makers to consider the relevance of this treatment according to their beacons and criteria.

Moreover, due to the differences in results found with this study compared with the previous economic analysis of the same treatment, this analysis underlines the importance and feasibility of adequate direct measurement of the various parameters required to fully undertake an economic analysis of a cancer treatment.

OP6. PRE-OPERATIVE STAGING OF RECTAL CANCER PATIENTS

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Colorectal cancer is the second most common cause of cancer death in the UK. In patients with rectal cancer local recurrence is an important cause of morbidity and mortality. The single most important factor affecting local recurrence is the degree of penetration through the bowel wall at the time of surgery. Hence the need for accurate pre-operative staging of the tumour. Endoluminal ultrasound (EUS) and digital rectal examination (DRE) are the currently accepted methods of pre-operative local tumour staging. Unfortunately DRE is often inaccurate and at least 20% of patients presenting with rectal cancer cannot be evaluated by EUS due to luminal narrowing as a result of tumours. MRI has the potential to evaluate all rectal cancers with high resolution and non-invasively. This project aims to compare the accuracy in staging of rectal tumours of MRI and EUS, and to establish a cost and outcomes model of the clinical impact of MRI in the care of patients.

One hundred patients diagnosed with colorectal cancer in South Wales were subject to pre-operative staging using the three methods and the results compared with histopathology. DRE was possible in 75 cases and gave the correct stage for 36% of cases. Using EUS, staging was possible in 56 cases and gave a correct outcome in 25% of cases. MRI staged all cases and correctly matched histology in 73% of cases.

Spearman's rho was used to test for correlation between outcomes. Of the three techniques only MRI resulted in a statistically significant correlation with histology. The correlation coefficient between histological outcome and MRI was 0.737.

The impact of inaccurate staging on resource utilisation and patient health related quality of life will be explored during the next stage of the project and will be available in the next few months.

OP7. THE EFFECT OF CANCER ON HEALTH PLAN SWITCHING AND PRICE SENSITIVITY

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In a market-oriented health insurance system, the willingness of consumers to switch health insurance plans in response to differences in plan premiums creates a strong incentive for plans and providers to control costs. However, if high risk individuals are less willing to switch plans or are less price sensitive than healthier individuals, consumer choice and plan switching may exacerbate the problem of adverse selection, contributing to market instability. In the extreme, adverse selection can cause certain types of insurance to disappear from the market and can reduce the incentives for improving the quality of care.

This study examines the effect of being recently diagnosed with cancer on the decision to switch health plans and on the sensitivity to premium differences across plans. The analysis is based on a five year panel data set that combines information on the health plan choices of University of California (UC) employees with information on cancer diagnosis and treatment from California's statewide cancer registry. The UC health benefits program merits attention because its design closely resembles leading proposals for reforming the US Medicare. The size of this data set—over 350,000 observations—makes it possible to obtain precise estimates of the effect of cancer on employee behavior. The results indicate that employees who were recently diagnosed with cancer or whose spouse has cancer are substantially less likely to change health plans than their healthier counterparts. The evidence also suggests that this difference contributed to severe adverse selection against one "high option" insurance plan.

OP8. EXCLUSION CRITERIA IN WILLINGNESS-TO-PAY - DO THEY MAKE A DIFFERENCE?

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Background

The use of the willingness-to-pay (WTP) method, as a means of valuing perceived health benefits, is increasing. However, theoretical arguments have been advanced, suggesting that values obtained from questionnaires or surveys may be subject to biases and inconsistencies. In particular, proponents of the method have suggested that certain sample data should be excluded *a priori* from WTP analysis in cases, for example, where a "protest vote" against payment has been recorded, where internal inconsistencies in response are evident and where a lack of understanding of the questionnaire has been manifested.

Objective

To test the sensitivity of WTP estimates obtained from survey results to the exclusion of data, as recommended in the literature.

Method

As a component of a randomised controlled trial of screening for colorectal cancer, WTP valuations were obtained from approximately 2 800 asymptomatic individuals. In addition, subjects provided (i) socio-economic, health status and health beliefs data and , (ii) a justification for selecting their particular WTP valuation. Two different WTP methods were employed with the sample, open-ended and payment scale. Average WTP was estimated for the restricted sample and re-estimated for the full sample, to test whether average estimated WTP for the sample changed significantly when "inconsistent" or "biased" records were excluded *a priori* on theoretical grounds.

Results

- The two different methods of eliciting values produced significantly different average WTP estimates.
- The a priori exclusion of certain classes of data on theoretical grounds appeared to exert little impact on the estimates of mean and median WTP.

Conclusions

- Theoretical concerns about WTP procedures may have less substance in practice, given a sufficiently robust sample;
- Observed anomalies or discrepancies may be as much a function of experimental design as of the WTP method itself.

OP9. ASSESSING THE IMPACT OF UNCERTAINTY BY USING BOOTSTRAP OTECHNIQUES WHEN COST AND OUTCOME DATA ARE CENSORED: A CASE STUDY OF CHEMOTHERAPY IN OVARIAN CANCER

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Background and objective: The analysis of uncertainty when individual patient data on costs and outcomes are available has recently received much attention for the case of binary outcomes. However, the principal outcome of interest in cancer clinical studies is patient survival time, possibly adjusted for quality of life. We demonstrate how stochastic uncertainty may be assessed, when outcome is survival and cost data are censored.
Methods: Censored cost data are analysed by the method proposed by Lin[1], estimating mean total costs per patient as a weighted sum of averages. The study period is subdivided into shorter intervals. For each of these, the weight is the estimated survival probability at the start of the interval and average cost is the observed average for the patients alive at the beginning. Mean survival is estimated by a restricted means analysis with the time point of restriction determined by statistical criteria. Applying these methods to the cost and outcome data of the patients in the evaluation yields a point estimate of the incremental cost effectiveness ratio (ICER). An estimate of the empirical distribution of the ICER statistic is obtained by using bootstrap re-sampling techniques.
Results: The method is illustrated by analysing cost and survival data collected in a RCT of chemotherapy regimens in ovarian cancer. The estimated empirical distribution of the ICER statistic in the cost-effectiveness plane allows calculation of the proportion of ICER estimates falling within any area of interest. Further, a cost-effectiveness acceptability curve to present the results of the analysis is derived. This curve indicates the probability that the more costly treatment will be considered cost-effective as a function of hypothetical values of society's willingness to pay for a better outcome.
Discussion: The proposed method takes account of stochastic uncertainty, when cost and outcome data are censored. Other types of uncertainty must be analysed by other means.

1 Lin DY et al. Estimating medical costs from incomplete follow-up data. Biometrics 53: 419-34, 1997

OP10. ESTIMATION OF UTILITY ASSOCIATED WITH PARTICIPATION IN CANCER SCREENING PROGRAMMES

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With conjoint analysis strength of preferences and willingness to pay for health care services - both particular attributes and specified service packages - can be elicited. It is possible with survey data to estimate stated utility as functions of effectiveness and side effects. However, the function values are subject to statistical uncertainty and benefit appraisals based only on mean utility values suppress this uncertainty and are at risk of inferring from chance rather than true differences in utility.

We propose a method to construct statistical confidence intervals for utility functions based on discrete choice or rank data in order to quantify the statistical uncertainty associated with utility estimates. The method applies bootstrapping with the (ordered) logit model often used to analyse data from discrete choice or ranks surveys in conjoint analysis. The health service is screening for respectively colorectal cancer and breast cancer. We focus on stated utility as functions of number of screen tests, effectiveness in terms of mortality risk reduction, risk of false positive outcomes, and of out of pocket payment.

The survey sample size was 764 50-year old men and women, the participation rate was 81%. The choice set up involved four options, non-participation or participation in one of three different screening programmes differing in efficacy, number of screen tests, risk of false positive test outcome and out-of-pocket expenditure. The 619 interviewees were requested to rank the four options. 20% was lost due to incomplete understanding of the hypothetical choice set up. The effective estimation sample comprised 483 men and women, whose stated ranks with ordered logit regression were related to attribute values, designed to vary over the sample, and to socioeconomic characteristics.

The implied WTP for a 1 percentage point reduction in cancer mortality risk is about 115,000 DKK, and WTP for 1 percentage point reduction in the risk of a false positive test outcome is about 1,250 DKK. Both WTPs are at median household income and both increase log-linearly with household income net of taxes. We calculated utility index values for screening programmes differing in terms of target age groups and screening intervals. However, the confidence intervals are fairly wide, in particular in one of the two logit specifications we applied, and it is only possible to distinguish statistically between the least and the most intensive screening programmes. For example the utility mean index value for breast cancer screening of 50-69-year old women every second year is 1.41 (95%CI=1.15-1.67) and every third year it is 1.26 (95%CI=1.02-1.50), so the 11% utility loss associated with the less extensive programme may be due to chance.

OP11. PREDICTING CANCER AGENCY EXPENDITURE FOR TRASTUZUMAB (HERCEPTIN®): THE CANADIAN EXPERIENCE

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Objective: To describe the costs of trastuzumab adoption for first-line treatment of metastatic breast cancer, from a provincial cancer agency perspective.
Methods: The national prevalence of breast cancer was estimated from *Canadian Cancer Statistics 1998* incidence and mortality rates. 26% were expected to represent metastatic disease. Literature values and expert estimates were used to determine the portion likely to receive chemotherapy in the next year. Expected yields for HER2 overexpression were drawn from primary literature. Dose (4mg/m^2 then 2mg/m^2 weekly), and length of therapy (29 weeks) were modelled from Phase III data. Only the trastuzumab cost was incremental; concomitant paclitaxel use was assumed to be unaffected. Products of each parameter's high, middle and low point estimates provided gross budget impact forecasts. The final estimates were adjusted for adoption rate factors (trial attrition, comparator use and reimbursement lag). Parameter estimates were confirmed with provincial agencies and consistent with treatment guidelines over a three-year horizon.
Results: Face validity was achieved with users in 7/10 provinces to date. Guidelines have been formally adopted in 3. The core model predicted that widespread testing would identify 564 patients nationally (range 155 to 1171). The incremental expenditure would be C$25,820 per case. The median national budget impact would be C$ 14.6M (range $C 4Mto $C 30M, mean $C 13.2M, 95% C.I.$5.3M–$20M). Four provinces would account for C$12 Mil.
Sensitivity Analyses: The estimates were most sensitive to reimbursement lag. The observed reimbursement lag was minimal upon registration. Provincial user uncertainty was greatest around comparator use. Minimal variance was attributed to other provincial differences, i.e., percentage treated and testing yield.
Conclusions: A transparent population-based model estimated the financial requirements of trastuzumab use that was consistent with Canadian provincial cancer agencies' guidelines. The model also showed how expenditures would reflect appropriate use.

OP12. THE IMPACT OF BREAST SCREENING ON FUTURE COSTS IN LIFE YEARS GAINED

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Background
The handling of future costs in life years gained is an area of debate in the methodology of cost-effectivness analysis. These health service costs may be quantitatively important for screening programmes where life years may be gained through screening and thus costs of treating other illnesses in life years gained incurred.
Methods
The Nottingham prognostic index (NPI) was used to predict the impact of breast screening on future health service costs (breast cancer and non-breast cancer costs). The NPI is a validated index incorporating size, stage and grade of breast cancer and is classifiable into four prognostic groups (PGs): excellent, good, moderate and poor. A cohort of 1,264 women was followed up for seven years after diagnosis. A Markov model was then used to extrapolate lifetime breast cancer and non-breast costs for each PG. Costs were discounted at 6%.
Results
Breast cancer costs increased as severity of prognosis increased (from £5,236 for the excellent PG to £8,892 for the poor PG). The opposite pattern was found for non-breast cancer costs (£5,259 for the excellent PG; £946 for the poor PG). The total cost (breast cancer and non-breast cancer cost) for each PG was very similar, at around £10,000. If costs are not discounted, the total cost for the excellent PG is approximately twice as much as the poor PG (£24,475 for the excellent PG compared to £10,932 for the poor PG).
Discussion
The inclusion of non-breast cancer costs in life years gained has a significant impact on the future costs associated with breast screening. Inclusion of non-breast cancer costs cancels out any potential savings in breast cancer cost resulting from better prognosis. If costs are undiscounted, an even stronger picture emerges with the future costs of better prognoses being twice as much as those of worse prognoses.

OP13. ECONOMIC EVALUATION OF NILUTAMIDE IN METASTATIC PROSTATE CANCER

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We estimated the cost-effectiveness of the treatment of metastatic prostate cancer with nilutamide plus orchiectomy compared with orchiectomy alone (OA) in patients with metastatic prostate cancer during the whole course of the disease.

The economic evaluation was based on data of an international clinical trial showing the advantage of nilutamide in terms of life saving. Full medical information was collected until patients stopped double-blind follow-up, then patients were followed until death but assumptions, based on expert's opinion, have to be made because of lack of information on medical management.

A standard cost approach was used. The setting of this study was that of the French Sickness Fund in 1996.

After 8.5 years of follow-up, nilutamide patients gained 183 days of life compared with OA patients. Benefit expressed in time without progression was 102 days. Estimated costs were 96,690F in the nilutamide group and 77,796F the OA group.

Cost per life year gained was then estimated at 36,687F.

Discounting and sensitivity analysis using a bootstrap method do not change dramatically the results.

Our study supports the use of nilutamide in the treatment of metastatic prostate cancer patients.

OP14. PAMIDRONATE IN CHEMOTHERAPY-TREATED BREAST CANCER PATIENTS WITH BONE METASTASES: IS IT COST-EFFECTIVE?

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Background: Biphosphonates are effective for preventing skeletal-related events in breast cancer patients with bone metastases, but their cost-effectiveness is still under debate. Two published studies in fact have yielded conflicting results, i.e. marginal cost-effectiveness of US $ 12,800 and 108,200 per quality-adjusted year of life (QALY), respectively.
Model: We used a decision analysis approach, considering two hypothetical cohorts of woman with metastatic, chemotherapy-treated breast cancer, undergoing pamidronate (90 mg every four weeks) or supportive therapy alone. We developed a 24-month-long Markov chain including 5 one-month-long health states related to bone metastases (chronic bone pain, acute vertebral fracture, acute nonvertebral fracture, post-vertebral fracture, post-nonvertebral fracture) and death. Probabilities of clinical outcomes were obtained from a randomized clinical trial (Protocol 19, Aredia Breast Cancer Study Group). Cost estimates were derived from local hospital charges and market cost of drugs. Quality of life was obtained by a structured time trade-off interview of 20 health care workers; the evaluated scenarios were described according to the EuroQol items. Cost-effectiveness was calculated from the perspective of the National Health Care System.
Results: Median survival of the modelled cohorts was 13.9 months. At baseline analysis, the cost was $3,919 in the pamidronate cohort and $2,243 in the supportive care one, while life expectancy was 112 and 99 quality-adjusted days, respectively. The incremental cost-effectiveness was $45,709 (IC 95%: 42,535-48,882) per QALY gained. Sensitivity analysis revealed that the results depended on the quality of life correlated with the primary disease and with pamidronate therapy, threshold values being 0.30 and 0.83, respectively.
Conclusions: Based upon the results of this analysis we can conclude that pamidronate is cost-effective in reducing bone complications in patients with metastatic breast cancer undergoing chemotherapy. The variation of the estimates among the three studies can be explained in terms of model and costs differences.

OP15. COST-EFFECTIVENESS ANALYSIS OF SENTINEL NODE BIOPSY VERSUS AXILLARY CLEARANCE AND SAMPLING

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Introduction: It is standard practice to undertake axillary clearance or sampling as part of the management of invasive breast cancer: 42% of premenopausal and 31% of postmenopausal women receive node clearance in the UK. This procedure has a risk of prolonged morbidity (e.g. arm swelling) and requires additional hospital stay. However, on average, only 25% of women are axillary node positive, in which case 75% of women, in retrospect, have an unnecessary operation. Sentinel node biopsy (SNB) is a new technology in which the sentinel axillary node is detected, and the removal of this single node facilitates accurate classification in 92-96% of cases.
Methods: We report on a cost-effectiveness analysis of SNB versus axillary clearance and sampling from a health service perspective. A decision model was developed in 2 parts: a decision tree for initial axillary surgery and adjuvant therapy; and a Markov model for subsequent prognosis. Clinical and resource use data were taken from the published literature and a pilot study of a UK trial. UK unit costs were used (1999 prices). Benefits were quantified as lifetime quality-adjusted life-years (QALYs) and separate sub-group analyses were undertaken based on menopausal status, fitness for chemotherapy and oestrogen-receptor status.
Results: As regards initial axillary management, the model shows that SNB has a lower expected cost (£1,273) than clearance (£2,674) and sampling (£1,934). The longer-term modelling quantified the importance of the SNB false negative rate (about 5%). For all sub-groups considered, SNB was found to be a dominant strategy over women's lifetimes, with lower costs and higher expected QALYs than clearance or sampling. This conclusion was robust to changes in most assumptions.
Conclusions: On the basis of best available evidence and under most assumptions, SNB is more cost-effective than axillary node clearance and sampling. A large clinical trial is planned in the UK to reduce uncertainty in key parameters.

OP16. COST-EFFECTIVENESS OF ADDITION OF EARLY HORMONAL THERAPY IN LOCALLY ADVANCED PROSTATE CANCER: RESULTS DECISIVELY DETERMINED BY CUT-OFF TIME POINT CHOSEN FOR THE ANALYSIS.

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Background and objective: Radiotherapy (RT) is the standard treatment of locally advanced prostate cancer. The present study aims to determine the cost effectiveness of adding early hormonal therapy to radiotherapy (COMB).
Methods: A retrospective cost effectiveness analysis has been carried out in relation to a randomized controlled trial of the addition to radiotherapy of early hormonal therapy with a LHRH analogue (goserelin). Data on resource use were collected retrospectively by examination of patient charts in one French hospital that recruited 90/415 patients in the trial. Mean survival is determined by a restricted means analysis, with the time point of restriction determined so that the standard error of the survival probability is $\leq 10\%$. Costs are assessed from the viewpoint of the French health insurance system, and are discounted at 3%. The problem of censored cost data is approached by the method proposed by Lin[1], and the impact of uncertainty is assessed by bootstrap techniques.
Results: The restriction time point is determined as 8.58 years. Assessed at this time, COMB engenders a gain in mean survival of 1.06 years and a reduction of the average total costs (ATC) of 12,700 FF. Prolonging the study period, the ATC of COMB relative to RT increase. For the longest observations available, the ATC of COMB are 81,700 FF, about 11,800 FF higher than for RT. But the gain in mean survival increases also, although it can not be estimated from measured data alone. At the point where ATC are equal, COMB increases mean survival by an estimated 1.23 years. Using extrapolation methods, the estimated survival benefit becomes 4 – 5 years.
Discussion: The analysis emphasizes the decisive importance of the method used to estimate mean survival and of the length of the study period chosen. The direction as well as the precise size of the estimated differences vary according to these choices.

OP17. HEALTH ECONOMICS OF TOMBOLA - TRIAL OF MANAGEMENT OF BORDERLINE AND OTHER LOW-GRADE ABNORMAL SMEARS.

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A recent review of the management of minor cervical abnormalities has suggested that there are no clear arguments, based on either cost or efficacy, that clearly favour any one particular management strategy [1]. Moreover, associated anxiety, health related quality of life and private costs faced by women under the alternate options remain to be evaluated. TOMBOLA is a pragmatic multi-centred randomised controlled trial which will fill the gap in current knowledge. In addition, TOMBOLA will assess the feasibility of using HPV testing as a triage method for women presenting with low-grade dyskaryosis.

The health economic objectives of TOMBOLA are:

- to determine health related quality of life in women managed according to either cytological surveillance or an initial colposcopy;
- to ascertain NHS resource use and specific costs to women and their families;
- to determine the value of HPV testing as a triage mechanism;
- to assess the long term implications of the alternative management strategies.

Patient specific cost and outcome data will be collected. In conjunction with specific psychosocial instruments to assess stress, anxiety and depression, general EUROQoL measures will determine health related quality of life. Data will be collected longitudinally over the three-year period of the trial at five pre-determined time-points. NHS resource use will be established through conventional methods via audit and database evaluation. Private costs will be assessed with a diary in addition to questionnaires administered at the time of secondary care interventions. Acceptability of private costs will be sought through focus group research. The long-term implications of the alternative management strategies and the impact of HPV testing will be assessed through mathematical modelling techniques and will assess the likely impact on (quality adjusted) life years. The trial began recruiting in December 1999 and the health economic assessment is due to begin in July 2000. Piloting of all health economic instruments is currently underway.

1. Baldauf, J. and J. Ritter, *Comparison of the risks of cytological surveillance of women with atypical cells or low-grade abnormalities on cervical smear: review.* European Journal of Obstetrics and Gynaecology, 1998. **76**(2): p. 193 - 199.

OP18. WILLINGNESS TO PAY FOR CANCER BREAKTHROUGH PAIN

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Objective: The main objective of this study is to estimate the monetary value of a new form of administering Oral Transmucosal Fentanyl Citrate (OTFC) for cancer breakthrough pain in patients receiving chronic palliative care. The new medicine will be compared with their present rescue medication. The problem with the usual treatment is that it takes at least half an hour to reduce the level of pain while with OFTC pain relief is almost instantaneous (5 min.).
Method: To estimate the monetary value of a reduction in the duration of pain the willingness to pay (WTP) method will be used in 130 cancer patients with episodes of breakthrough pain. They will be interviewed by their usual doctor. WTP questions will be asked using the open card method and internal consistency will be assessed in several ways. First, we will see if WTP is related with the subjective feeling of pain of each patient. The subjective feeling of pain will be obtained using Likert-type scales for pain. Second, preferences for a reduction in pain will be also estimated using the Standard Gamble. Although the main objective of the study is to estimate the monetary value of pain reduction, the Standard Gamble (SG) questions will be used to estimate the internal consistency of WTP estimates. In this case, we will present a lottery where the certain option is usual treatment, success is defined as minimum duration of pain and failure as 1 more hour of pain than usual. The method used to ask SG questions is the Probability Equivalent. We will try to establish a correlation between preferences measured using SG and WTP. Sociodemographic and clinical characteristics will also be obtained from patients.
Results: We are now in the process of collecting data. Data will have been collected by the end of June.

OP19. ETHICAL, MEDICAL, ECONOMICAL AND JURIDICAL SIGNIFICANCE OF THE DIFFERENTIATION BETWEEN PHYSICO-CHEMICAL AND PSYCHO-SOCIAL TREATMENT EFFECTS: DISCUSSING THE RESULTS OF OUR COCHRANE REVIEW "IMMUNOTHERAPY OF ADVANCED RENAL CELL CANCER".

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Initiated and chaired by CC we completed a quantitative meta-analysis (Cochrane Review) on "Immunotherapy of Advanced Renal Cell Cancer" to test two hypotheses: "Treatment with interferon alfa prolong survival in patients with advanced renal cell cancer" and "Treatment with high dose interleukin-2 prolong survival in this group of patients". Based on response rates from 42 eligible randomized studies and on survival data from 26 studies the results seem to confirm that interferon alfa can indeed prolong survival in patients with advanced renal cell cancer. In a further analysis of the data four observations were made which suggest a differentiated interpretation of the observed effects.
1. Significant differences were seen in response rates and in survival when immunotherapies were used as experimental treatment and non-immune therapies as controls. 2. These differences were not seen when experimental immunotherapies were compared with other immunotherapies as controls, i.e. any kind of immunotherapy – whether used as experimental or control - produced a favourable outcome. 3. In contrast, we observed significant differences (in response rates and survival) between experimental and control groups if the experimental group but not the control group received immunotherapy. The unexpected observation was the „inverted vector" of the response: Instead of a more favorable result of the effective experimental immunotherapy it was the less favorable result of the non-immune control treatment which produced the significant difference. 4. In a blinded experi-ment placebo produced the same favorable responses like the experimental immunotherapy, i.e. there was no significant difference.
Two conclusions are drawn from our observations. First, the observed survival advantage cannot be explained by physico-chemical effects. The data suggest that framing the physician's and patient's knowledge about treatment seems to be a rather important factor in medical interventions. This factor has to be investigated to meet ethical, medical, economical and juridical demands.

OP20. COMPARISON OF MARGINAL AND AVERAGE COSTS OF CHEMOTHERAPY IN HOSPITAL AT HOME VERSUS STANDARD HOSPITAL CARE.

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Objective : To compare the costs of anti-cancer chemotherapy in hospital at home versus standard hospital care in a French area.
Methods : This study is based on a randomised controlled crossed trial, which included 42 patients for whom chemotherapy cycles were alternatively given in both settings. All cost categories were taken into account, comparing those associated with hospital admission for chemotherapy versus the same treatment in hospital at home. A detailed assessment was performed for coordination and care in both structures, regarding marginal costs and average costs, from the viewpoint of society.
Furthermore, theoretical costs were computed for hospital at home, valuing drugs at the same level (hospital level) for both structures. It allows us to asses "social costs", avoiding the bias due to fixed drug prices which, in France, differ from a structure to an other. Data were compared with the Wilcoxon test and adjusted for 1998 Euros (€).
Results : There is a highly significant difference (p=0.001) between marginal costs in home care (258.7€ for one infusion of chemotherapy) and hospital care (152€). Conversely, difference between average costs is not significant: 281.1€ for home care and 286€ for hospital care. Drug prices associated with home care (152.6€) are significantly different from those in hospital (82.6€) (p=0.001). Using the theoretical approach, only home care costs change. Marginal costs remain significantly higher for home care (188.7€ versus 152€, p=0.05) while in terms of average costs, home care is significantly cheaper than hospital care (211.1€ versus 286€, p=0.001).
Conclusion: The results show that the interest of developing home care in anticancer chemotherapy is questionable as regards costs. In the French health-care system, where there is an excess of hospital beds, marginal costs seem to be more relevant indicators than average costs. Of course, outcomes must be considered as well, specially regarding patients preferences.

OP21. GEOGRAPHIC DELIVERY MODELS FOR RADIOTHERAPY SERVICES

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Purpose: This study was undertaken to compare the societal cost of centralised and distributed radiotherapy service provision for idealised urban and rural populations. Societal cost encompasses institutional expenditures and patient costs which, for this analysis, include time costs based on the human capital approach.
Method: Institutional costs were determined using an activity costing spreadsheet which we have developed and employed extensively in previous studies. Patient costs were estimated using published Canadian travel, salary and patient age data. The urban model consists of a population of 2.3M (approximately the population of Toronto) uniformly distributed over an area of 460 km^2 with radiotherapy services provided either by a central 14 machine facility or a 4 machine comprehensive facility with 10 peripheral satellite sites providing treatment only. The rural population consists of 640,000 people (approximately the population of Northeastern Ontario) and is divided between two nodes of 480,000 and 160,000 separated by a distance of 300 km. Radiotherapy services are provided by either a central, 4 machine facility at the larger node or a 3 machine site with one satellite treatment only machine at the smaller node. In all scenarios, patients travel to the central site for assessment, treatment preparation (e.g. simulation) and follow-up.
Results: From the societal perspective, distributed radiotherapy in the urban setting was slightly (10%) cheaper than centralised delivery. For the simplified rural model with the population concentrated in two nodes, separated by 300 km, distributed radiotherapy was also cheaper (15%) than centralised delivery. Savings in societal cost accrue to the patients at 25% (urban) and 35% (rural) when distributed service provision is compared with centralised.
Conclusion: Distributed radiotherapy is economically advantageous in both the urban and rural models when viewed from a societal perspective. Reduced patient costs can enhance accessibility to radiotherapy.

Acknowledgment: Northern Cancer Research Foundation.

OP22. CHEMOTHERAPY AS PRIMARY TREATMENT IN ADVANCED COLORECTAL CANCER: ECONOMIC EVALUATION OF THREE DIFFERENT 5-FU SCHEDULES

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Background and objective: Chemotherapy with *bolus* 5-FU modulated with folinic acid (5-FU + FA) is considered standard primary treatment for patients with advanced metastatic colorectal cancer. More recently interest has focused on *infusional* 5-FU, which has another mode of action and different pattern of toxicities. The present economic evaluation compares infusional and bolus 5-FU regimens.
Methods: In a multi-center RCT, 497 untreated patients were randomized between infusional 5-FU + FA (arm A), the same dose of infusional 5-FU without modulation (arm B) and bolus 5-FU + FA (arm C). Data on the use of medical resources, comprising hospital stays and visits, concomitant medications, transfusions and treatments after progression, were collected prospectively during the trial. The cost assessments will use Dutch and German (90% of the trial patients) unit cost data.
Results: Overall survival is equivalent, while progression free survival is significantly increased in arm A (median 6.4 months). This benefit is associated with more toxicity, mainly diarrhea[1]. The average number of days spent in hospital is 21 in arm A versus 24 in the other arms. Other types of resources are used to the same extent in each arm, except that the number of blood transfusions per patient is somewhat higher in arm C than in A and B.
Discussion: A complete cost analysis, correcting for censored cost data, will be presented at the meeting, with costs determined from the viewpoint of the Dutch and German health insurance systems, respectively. As large variations are observed between institutions with regard to number and length of hospital admissions, a mixed model approach will be used to examine the effect of treatment on days of hospital stays.
Discussion: Infusional 5-FU + FA is equivalent to standard treatment with regard to survival, while engendering a reduction in the number of hospital days. The overall effect on costs remains to be determined.

1 Schmoll H-J et al. Weekly 24h infusion of high dose (HD) 5-fluorouracil (5-FU) with or without folinic acid (FA) vs. bolus 5-FU/FA (NCCTG/Mayo) in advanced colorectal cancer (CRC): A randomized phase III study of the EORTC GITCCG and the AIO. ASCO Proceedings 2000

OP23. ECONOMIC EVALUATION OF REDUCING THE INTENSITY OF CHEMOTHERAPY IN GOOD PROGNOSIS TESTIS CANCER PATIENTS IN THE NETHERLANDS

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Background and objective: Testicular cancer has become one of the most curable solid neoplasms thanks, inter alia, to effective cisplatin based chemotherapy combinations. Many of the current efforts are therefore directed at finding equally effective, but less toxic chemotherapy regimens. This study presents an economic evaluation in relation to a clinical trial assessing the impact of reducing the number of cycles of standard chemotherapy administered to good prognosis testis cancer patients.
Methods: The clinical trial (MRC-EORTC30941) was designed as a 2 x 2 factorial trial comparing 3 cycles of bleomycin, etoposide, cisplatin (3BEP) versus the standard 4 cycles (3BEP-1EP) administered over 5 days versus 3 days. Data on resource utilization were recorded in the case report forms of the trial and comprise hospital stays and visits, concomitant medications, blood transfusions and treatment after progression. These have been supplemented with data extracted from patient charts in selected institutions. Costs are determined from the viewpoint of the Dutch health insurance system.
Results: The clinical analysis[1] concludes that 3BEP is equivalent to the standard therapy in terms of progression free survival, which is approximately 90% at 2 years. The preliminary cost determination presented here focuses on days of hospital stays, as the use of other resources has been very limited or inadequately documented (concomitant medication). Patients are hospitalized during administration of chemotherapy. Additional hospital stays due to adverse events vary from 1.8 day/patient, in the group receiving standard therapy over 5 days to 3.0 days/patient for those given this treatment over 3 days.
Conclusion: Complete cost data will be presented at the meeting. The reduction in days of hospital stays from giving 3BEP over 3 days compared to standard therapy is about 10 days. This cost reduction is not likely to be offset by increases in other costs, as the use of other resources observed is strictly limited.

1 De Wit et al. Final analysis demonstrating the equivalence of 3 BEP vs. 4 cycles and the 5 day schedule vs. 3 days per cycle in good prognosis germ cell cancer. An EORTC/MRC phase III study. ASCO Proceedings, 2000

OP24. COST-EFFECTIVENESS OF LIPOSOMAL AMPHOTERICIN B FOR THE EMPIRIC TREATMENT OF FEVER OF UNKNOWN ORIGIN IN BONE MARROW TRANSPLANT PATIENTS: A DECISION ANALYSIS

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PURPOSE: To compare the effectiveness and costs of two strategies for the empirical treatment of fever of unknown origin because of suspected invasive fungal infection (IFI) in bone marrow transplant (BMT) patients namely, empirical treatment with amphotericin B desoxycholate (DC-Amb), followed by liposomal amphotericin B (L-Amb) in case of treatment failure or nephrotoxicity (strategy DC/L-Amb) versus first line treatment with L-Amb (strategy L-Amb).
MATERIALS AND METHODS: A decision analytic model was developed and effectiveness and costs for both strategies were calculated and compared. Estimates for the probability variables for successful treatment, treatment failure and the occurrence of side-effects were derived from published reports. Effectiveness was expressed as survival to hospital discharge. Drug costs and the costs associated with the treatment of side-effects were determined according to the perspective of the health-care system. Probabilistic sensitivity analyses were performed using both probability and cost variables to analyse the simultaneous impact of the variables on the study findings.
RESULTS: Baseline analysis showed the increase of probability of survival from 77% for the L-Amb strategy to 85% using the DC/L-Amb strategy. The expected cost of L-Amb was USD 27,810 per patient compared to USD 12,776 per patient for the DC/L-Amb strategy. The incremental cost per life saved was nearly USD 183,000. The probabilistic sensitivity analysis showed the model to be highly sensitive to the costs of L-Amb per day revealing that if the cost of L-Amb per day is less than USD 122, L-Amb is more effective expressed in lives saved at a lower cost compared to the DC/L-Amb strategy.
CONCLUSION: The L-Amb strategy results in a higher survival to hospital discharge. The expected costs are higher compared to DC/L-Amb strategy. Probabilistic sensitivy analyses show that accurate data on the efficacy of L-Amb after DC-Amb failure are lacking but are important to the cost-effectiveness of the DC/L-Amb strategy.

OP25. COST-EFFECTIVENESS (QUALITY ADJUSTED LIFE YEARS) OF GOSERELIN ACETATE COMPARED TO ORCHIECTOMY IN THE TREATMENT OF PROSTATE CANCER

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AIM: We evaluate from the perspective a Canadian Regional Cancer Agency the comparative cost-effectiveness of a LHRH and orchiectomy in the treatment of patients with stage D_2 prostate cancer. METHODS: We use data from a large randomized clinical trial comparing the efficacy and safety of goserelin acetate to orchiectomy. Quality adjusted survival was the primary measure of effectiveness; survival was adjusted by utility weights to reward disease and toxicity free survival while penalizing time with toxicity and the psychosocial impact of orchiectomy. Cost data are Canadian prices. Utilities are obtained from published literature. Threshold utilities are also evaluated.
RESULTS: The median quality adjusted survival *without* adjustment for the psychosocial impact of physical castration was 102 weeks in the orchiectomy group compared to 111 weeks in the goserelin acetate group, yielding an increase in survival favoring patients treated with goserelin acetate of 9 weeks or 0.17 years. As the utility weights associated with the disutility of physical castration were applied, the incremental quality adjusted survival benefits favoring goserelin acetate increased to 24 weeks or 0.46 years with 0.85 as the weight. The median cost of goserelin acetate in this trial was $3,230. The median cost of an orchiectomy in Canada was $1,690 yielding an incremental median cost of $1,540 with a standard deviation of $3,515. When no adjustment is made, the 95% confidence interval for the cost per gain in quality adjusted life year was $2,170 and $15,948. With adjustments for the psychosocial impact of orchiectomy, the cost-effectiveness results simply improve and achieve statistical significance at the 5% level with a weight of 0.88. The 95% confidence intervals are (-$3,541) and $10,237.
CONCLUSION: Thus, goserelin acetate is a *highly cost effective* alternative to orchiectomy in patients with advanced and metastatic prostate cancer.

OP26. COST-EFFECTIVENESS OF ANASTROZOLE COMPARED TO TAMOXIFEN IN THE TREATMENT OF POST-MENOPAUSAL WOMEN WITH BREAST CANCER

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Two large randomized clinical trials have established the comparative clinical efficacy and safety of anastrozole as an alternative to tamoxifen in the treatment of post menopausal patients with breast cancer.
AIM: We conduct a cost-effectiveness analysis based on the combined clinical trial data from those two large randomized comparative trials where effectiveness is the quality adjusted time to disease progression, the primary clinical endpoint.
METHODS: We used the clinical trial data from trial 0027 and 0030 that compared the efficacy and safety of anastrozole to tamoxifen in postmenopausal women. Time of disease progression was defined as the appearance of any new lesion or an increase in the sum of measurable lesions or worsening of non-measurable disease. Treatment related toxicities were defined a priori. Time spent with treatment related toxicities was subtracted from disease progression free time and quality adjusted with a utility weight of 0.5. We also varied the utility weight of toxicity time by severity of the toxicity. Time without disease progression or toxicities was quality adjusted as unity. Kaplan Meier estimation was adjusted for baseline lesion size, age, receptor status and prior hormonal therapy. Costs consist of Canadian drug costs applied to the actual dose received.
RESULTS: Adverse events were statistically similar between groups although the frequency of thromboembolic disease was clinically significantly higher in the tamoxifen group with an unadjusted p-value of 0.0487. That analysis indicated that patients who are treated with anastrozole instead of tamoxifen can expect to enjoy a median increase of 1.67 months ($p<0.05$) in their quality adjusted time to disease progression. The comparative cost-effectiveness was $7,824.24 per QALY with a 95% lower bound estimate of $14,774.56.
CONCLUSION: Anastrozole compared to tamoxifen is a highly cost-effective first line agent in the treatment of advanced staged breast cancer.

OP27. ECONOMIC MODEL OF SCREENING FOR LUNG CANCER

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Introduction: The development of low dose helical CT (LDCT) scanning to detect nodules as small as a few millimeters has sparked renewed interest in LC screening.
Objective: To model the cost-effectiveness of LC screening, based on available results of recent studies and cancer registry data.
Methods: This decision analysis model examines a baseline prevalence screen with subsequent annual screens for 5 years. We used the SEER public-use database for estimates of LC incidence (1990-96) (~270/100,000), and survival stratified by gender, age group, LC stage, and for Stage I, tumor size (1973-1996). Total LC prevalence in a high risk group of smokers between 60 and 74 years of age (2700/100,000), tumor size distribution at detection for Stage I disease, cancer detection rate and follow up testing for a LC screening program were estimated from baseline results of the ELCAP study reported by Henschke et al., 1999. All patients in the hypothetical screened cohort had a LDCT scan, and patients with positive results were followed by high resolution CT (HRCT), and subsequently recommended for biopsy, follow-up HRCT, or no follow-up. The model assumes that patients with a certain size tumor have the same survival experience independent of detection method, an assumption potentially susceptible to length-time bias. Cost estimates were published stage specific average annual Medicare payments, and screening test costs were based on 1999 national Medicare reimbursement data. Cost-effectiveness ratios were calculated over 5 years, and discounted at 3%.
Results: In this population , annual screening over 5 years under the model assumptions appears to be cost-effective at about $19,000 per life year saved. If a 1 year lead time bias is factored into this calculation, screening would still be considered cost-effective at $57,752 per life year, but if the lead time bias is any greater, the life year benefits of screening are eliminated.

OP28. TOXICITY AFTER CONFORMAL RADIOTHERAPY OF THE PROSTATE MEASURED BY THE EORTC QUALITY OF LIFE CORE QUESTIONNAIR QLQ-C30 AND THE NEW EORTC-PR25 PROSTATE MODULE AND A COMPARISON WITH THE LENT-SOMA TOXICITY SCALE

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Introduction:
Treatment-related toxicity and its influence on quality of life (QOL)-matters are becoming increasingly important in treatment decisions. We studied general and disease-specific QOL, as measured by the EORTC-QLQC30 and the PR-25 prostate-cancer-module, after conformal radiotherapy (RT) to the prostate. Additionally, the accuracy of the physician graded LENT-SOMA toxicity scale was evaluated.
Methods:
50 consecutive patients, irradiated with external beam RT only. Median age 70 years (range 54-81yrs). Doses: 66.6-72.0 Gy; 1.8 Gy fractions. Anti-androgen therapy in 24%. The EORTC-QLQ-C30 (version 3.0) core questionnaire and the EORTC-QLQ-PR 25 prostate cancer module were mailed to all 50 patients. Within six weeks of filling out the questionnaires, chronic rectal toxicity was additionally graded in 31/50 patients according to the LENT-SOMA grading system, using the subjective and management criteria.
Scoring of the QLQ-C30 was compared to a general Norwegian population (60-69yrs).
Results:
Median follow-up 8 months (3-20). Mean scores:
QLQ-C30 (88% responders): Global health status/QOL: 79.2. Except for diarrhea (25.0, Norwegians 7.8), our patients showed a lower degree of symptoms or higher degree of functioning for all items.
PR25 prostate-module (86% responders): Sexual symptoms: 39.1, bowel-symptoms: 12.2, urinary-symptoms: 17.7.
Significant correlation was found between QOL and all general functioning domaines, bowel-, treatment related- and sexual-symptoms, enjoyment of intercourse, ejaculation, pain, fatigue.
Transformation of the LENT SOMA-toxicity scale (n=31) into a linear scale and comparison to prostate-module: Difference LENT-SOMA/modulebowel symptoms: Difference 5.1; bladder-symptoms: difference 7.8.
Conclusion:
After RT of the prostate, QOL and general non-treatment related symptoms and functioning were not compromised. In contrast to bowel-and sexual-symptoms, which were correlated to QOL, but not urinary symptoms. The LENT-SOMA-toxicity scale accurately represents bowel and urinary symptoms.

OP29. COSTS AND QUALITY OF LIFE OF PATIENTS UNDERGOING PERIPHERAL BLOOD STEM CELL TRANSPLANTATION OR AUTOLOGOUS BONE MARROW TRANSPLANTATION FOR REFRACTORY OR RELAPSED HODGKIN'S DISEASE OR NON-HODGKIN'S LYMPHOMA.

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OBJECTIVE: To assess costs and quality of life of patients undergoing peripheral blood stem cell transplantation (PBSCT) and patients undergoing autologous bone marrow transplantation (ABMT) for refractory or relapsed Hodgkin's disease or non-Hodgkin's lymphoma, after having responded to second-line induction chemotherapy. DESIGN: In this multicenter randomized clinical trial, 119 patients were randomized to receive either PBSCT of ABMT (proportion 2:1). Full costs were determined from the start of the second-line chemotherapy up to three months after discharge of the transplantation hospitalization, based on all data stored in the hospital information system and the medical records. Quality of life was measured by the EuroQol, the Rotterdam Symptom Checklist (RSCL) and the SF-36 at three times: on the day before transplantation, 14 days after the transplantation and three months after discharge. RESULTS: Of 98 transplanted patients, 68 underwent PBSCT and 30 ABMT. Costs of the induction chemotherapy were € 11180. Costs of the transplantation period (including leucapheresis or bone marrow harvesting) were significantly lower in the PBSCT group (€ 20468) than in the ABMT group (€ 25339; P<0.05). Costs of follow-up (three months) were € 2090 for PBSCT and € 3088 for ABMT. With respect to quality of life, significant differences emerged on the RSCL. Fourteen days after the transplantation, ABMT patients reported more complaints concerning tiredness, lack of energy, headache, dizziness, palpitations, rash, sweating and shivering and the physical complaints sum score was higher than in the PBSCT group. Three months after discharge, ABMT patients reported more compaints about nausea, vomiting and shivering. No significant differences to the disadvantage of PBSCT occurred. CONCLUSIONS: PBSCT is correlated with lower costs and a better quality of life than ABMT for patients with refractory or relapsed Hogkin's disease or non-Hogdkin's lymphoma.

OP30. THE RESOURCE IMPLICATIONS OF EXTENDING THE ROUTINE INVITATION TO BREAST SCREENING TO WOMEN AGED 65-69 YEARS

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UK breast screening policy currently restricts routine three-yearly invitation to screening to 50-64 year olds. An extension of the age range to include 65-69 years old women is currently considered. Because uptake by the older age group may be lower the increase in demand for breast screening is uncertain. This paper uses econometric techniques to predict the additional demand for breast screening. The predictions will be used to determine the resource implications of such a policy.

A demonstration project was run where a sample of 1015 women aged 65-69 was invited for breast screening. The binary choice did or did not attend is modelled using probit regression. The independent variables include (i) the woman's characteristics: her age; the deprivation score of the area she lives in; her screening history and (ii) the characteristics of the screening: whether the screening took place in a mobile van or at a static site. The robustness of the model is examined by modelling the most recent attendance of women aged 60-64 in the same area (n=1,000) and in two other regions in Scotland (n=3,000).

The modelling of attendance is quite successful. The attendance decision is correctly predicted for about 85% of the women. The model is better at predicting attendance than at predicting non-attendance. Previous screening history appears to be the main determinant of attendance and the impact is similar across age groups and regions.

The model is used to predict additional demand for the whole of Scotland. Confidence can be placed on these predictions since the predictive ability and the robustness of the model are both satisfactory.

OP31. EARLY WITHDRAWAL FROM CERVICAL CANCER SCREENING: WOULD IT BE COST-EFFECTIVE?

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Background and Objective
Sherlaw-Johnson and colleagues [1] examined the likely resource impact of withdrawing women early from screening using a mathematical model and suggested that although two additional cases of invasive cervical cancer per 100 000 women per annum would result, substantial resource savings could be made. We present here predictions of the likely cost savings relative to estimates of life year losses as a result of early withdrawal from screening.

Methods and Results
The model presents estimates of the expected annual incidence per 100 000 women and required number of screening procedures under two withdrawal scenarios: withdrawal at either 50, 55 or 60 after three consecutive negative smears; or withdrawal after the same specified ages after a negative smear and a simultaneous negative HPV test. Using estimates for routine cytology, for both positive and negative colposcopic investigation and further treatment in addition to estimates of the likely cost of HPV, the total expected cost of early withdrawal can be estimated. Outcome data, originally expressed as additional cases of invasive cancer have been extrapolated by estimating median survival so that *'reverse'* cost effectiveness ratios, namely expected cost savings per life year sacrificed, can be derived. Given the assumptions of the model the maximum incremental savings amount to less than £10,000 per additional life year lost each year.

Conclusion
Withdrawing women early from screening can only be cost-effective if low values are placed on life year losses. Given the National Health Service is currently funding treatments costing thousands of pounds per life year gain it seems unlikely that it would wish to sacrifice other life years to gain a lesser amount in return.

1. Sherlaw-Johnson, C., S. Gallivan, and D. Jenkins, *Withdrawing low-risk women from cervical screening programmes: mathematical modelling study.* BMJ, 1999. **318**: p. 356 - 361.

OP32. CANADA'S POPULATION HEALTH MODEL (POHEM): A TOOL FOR PERFORMING ECONOMIC EVALUATIONS OF CANCER CONTROL INTERVENTIONS

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Since 1990, Statistics Canada has collaborated with medical experts to develop a microsimulation model of the health of the Canadian population. The Population Health Model (POHEM) now contains complete disease – costing modules for lung and breast cancer, as well as less detailed modules for other diseases. The cancer costing modules were designed to reflect Canadian risk factors, incidence, initial diagnostic and therapeutic cancer management practices, survival probabilities, and treatment at disease progression.
The objective in developing individual disease modules was to replicate "current" or "standard" diagnostic and therapeutic practice in order to develop a baseline scenario.
Once the baseline scenario was established, the impact of alternative strategies for prevention, early detection or new therapeutic approaches was evaluated. Lung and breast cancer examples follow.
Prior to the development of the lung cancer module in 1993, standard management of advanced non-small cell lung cancer had been best supportive care, which involved a minimal amount of palliative radiotherapy. Since then, chemotherapeutic interventions have been used to extend survival. POHEM was useful in performing cost-effectiveness analyses of these chemotherapy regimens. This information has been helpful in assuring policy makers that these treatments are cost-effective relative to other health care interventions and, therefore, worth adopting. A cost analysis was used to support a business case for an outpatient lung cancer diagnostic unit to provide timely, efficient, high quality cost-effective diagnostic care.
In addition to documenting the current practices and the burden of breast cancer in Canada, the breast cancer module has been used to evaluate the impact of the following interventions: reducing length of hospital stay for initial breast cancer surgery; providing locoregional radiotherapy following mastectomy; and providing tamoxifen to women at high risk of breast cancer. The results of each evaluation will be discussed in terms of recommendations provided and their relevance to decision-makers.

OP33. A SIMULATION MODEL OF POLYP GROWTH RATE AND ITS USE IN ESTIMATING THE EFFECTS OF CHEMOPREVENTION ON THE COST-EFFECTIVENESS OF DIFFERENT POLYP SURVEILLANCE FREQUENCIES

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Problem: Chemoprevention can reduce polyp arrival/growth rates and CRC. Existing models are based on current polyp growth rates, not allowing for detailed analysis of chemoprevention effects on polyps. Cost effectiveness analyses of chemoprevention will require a model such as this where growth can be varied.

Methods: We developed a stochastic simulation model for a cohort of 50-60 year olds which simulates arrival and growth of polyps as a function of empirically estimated parameters from observational studies in human populations. The model is used to predict size distribution of recurrent polyps annually for 10 years after initial colonoscopy/polypectomy and measure effects of different intervals of colonoscopic surveillance, accounting for miss rate, arrival, and growth rate of recurrent polyps for 4 risk groups. We vary arrival and growth rates to estimate number and size of polyps, malignant polyps, and cases of CRC. The model is validated by two different methods. Costs were determined for colonoscopies, and CRC treatment; and life years saved using SEER survival data. Cost per life year saved of different surveillance frequencies, given various estimates of polyp arrival and growth rates for 4 risk groups was estimated.

Results: We compared clinical outcomes for base line estimates using normal growth rate distributions compared with arrival and growth rates which are reduced by 10% and 25 %. For risk group 3, the number of malignant polyps in a population of 500 were 1.019 vs 0.215 for exam at year one, 12.8 vs 1.195 for year 5 and 39.2 vs 2.9 for year 10; and number of CRCs avoided were 7 vs 0.7 at year 5 and 21 vs 1.6 at year 10 for normal vs 10% reduced growth rates respectively. Deaths avoided were 2.7 vs 0.26 for exam at year 5 and 7.7 vs 0.59 at year 10 for normal vs reduced growth rates. The cost-effectiveness varied depending on the frequency of colonoscopy and risk group, but was cost effective in highest risk groups at about 3 to 4 year examination intervals.

OP34. WILLINGNESS-TO-PAY FOR COLORECTAL CANCER SCREENING: FAECAL OCCULT BLOOD TESTING *VS.* FLEXIBLE SIGMOIDOSCOPY

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Background
Cancer of the colon and rectum is one of the most common cancers in the USA and Europe. The disease has an established stage progression and the observed close association between stage at detection and post-diagnosis survival justifies early intervention. As the earliest stages of the disease tend not to present symptomatically, it has for some time been thought that mass population screening programmes would prove effective in reducing mortality. A variety of screening protocols are feasible, although only two have been the subjects of major trials in the UK - biennial faecal occult blood testing (FOB) and once-only flexible sigmoidoscopy (FS). Likely public response to either protocol, beyond that of the trial populations, is presently unknown.
Objective
To obtain valuations of both FOB and FS screening, from an asymptomatic, unscreened population, using the willingness-to-pay (WTP) approach.
Method
Two WTP instruments (open-ended *vs.* payment scale) were completed by approximately 2 800 subjects, drawn from across east-central England. In addition to WTP responses, we obtained socio-economic, health status and health beliefs data for each subject.
Results
The WTP data permit the construction of a demand curve for cancer screening, by each of the protocols. For each protocol, the resulting curve approximated to a rectangular hyperbola, a form commonly encountered in demand estimation generally. In fact, the two demand curves lay very close to one another, with median WTPs for each modality in the range £30 to £50, depending on the instrument. As would be predicted from economic intuition, individual WTP varied with income and education level, health beliefs and health behaviour.
Conclusion
- Despite individuals expressing clear preferences for one protocol rather than another, neither protocol was clearly preferred by the sample in aggregate.
- The average expressed WTP for screening was more than the actual resource cost of the testing.

OP35. PROSTATE CANCER SCREENING – A COST-EFFECTIVENESS MODEL

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Background
Screening for prostate cancer is controversial, with no data from completed randomised control trials on the effectiveness and cost-effectiveness. We have developed a decision-analytic model of prostate cancer screening to aid discussions on whether to fund a UK based trial of prostate cancer screening.
Objectives
- To assess the cost-effectiveness of screening for prostate cancer. The baseline option consists of a biennial screen, involving a mailed invitation to attend a GP for a serum prostate specific antigen (PSA) test for males aged 55-69 years.
- To highlight critical and uncertain parameters in the model, which could be answered by a UK trial of prostate cancer screening

Method
The overall model consists of two parts, which together simulate the likely costs and effects of a prostate cancer-screening programme:
1) a cancer-detection model, which takes the form of a spreadsheet-based decision tree.
2) a 7-state Markov model simulating disease progression and the costs and effects of treatment. Patients progress in annual cycles until dead from prostate cancer or from other causes. To compare the impact of a screening programme with the alternative of no screening, the model is replicated with parameter values representing current levels of detection and treatment. Model parameters have been taken from published literature sources for the prevalence round and subsequent incidence rounds.

Results
The model has highlighted a number of critical and uncertain parameters:
- Uptake rate
- Sensitivity and specificity of PSA test by age and stage of disease
- Stage distribution at diagnosis for screen detected and symptomatically presenting cancers
- Progression rate's by treatment modality and disease stage
- Rate of interval cancers
- Utility values

Conclusion
The economic evaluation using decision analytic modelling has provided important information for the design of a randomised control trial of prostate cancer screening. It has identified critical variables necessary for the evaluation of the trial and the economic analysis.

OP36. A COMPARISON OF TIME TRADE-OFF AND STANDARD GAMBLE HEALTH STATE UTILITY MEASUREMENT IN OESOPHAGEAL CANCER PATIENTS

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Background: Patients with oesophageal cancer have to make choices involving trade-offs between quality of life, length of life and side effects of treatment. However research on medical decision making and health state preferences of patients with oesophageal cancer is limited. This study serves to address this deficiency and describes the results of a comparison between patient based values using different elicitation techniques.
Objective: Assess concordance of health state values using time trade-off and standard gamble techniques with patients who have had curative surgery for oesophageal cancer.
Design: Face to face interviews using structured interview techiniques and graphical aids. Respondents randomised to value health state utilities using either standard gamble or time trade-off method.
Setting: Northeast England.
Participants: 60 disease free patients who have previously had curative surgery for oesophageal cancer.
Outcome Measures: Health utility values from time trade-off and standard gamble.
Results: Data will assess the feasibility of using health state valuation on patients with oesophageal cancer and explore the extent to which changes in health outcome and treatment provide different health state values. A comparison will also be made determining whether standard gamble and time trade-off techniques provide different health state values.

Data will be available in July.

PP1. THE CANCER PAIN ECONOMIC MODEL

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Objective: To design a model that educates clinicians and health care policy decision makers about the burden of cancer pain in their individual health care population, and assists them in weighing the relative efficacy and cost of different strategies of cancer pain management.
Design: A tailored cost-effectiveness analysis using a decision analytic model.
Intervention: A computerized educational tutorial that includes a cancer pain economic model where three cancer pain management strategies are compared, (1) guideline-based care, (2) oncology-based care, and (3) usual care.
Measurements: Efficacy of the relative strategies and the cost of medications plus procedural interventions over a one-month timeframe. Users can tailor the inputs for population demographics and resource costs.
Results: Of 100,000 patients in a health care organization, 503 will have cancer and 214 will suffer from cancer pain. After one month, the percentage of cancer pain patients with effective pain management and the cost of each of the strategies are as follows: (1) guideline-based care, 85% and US$433.35, (2) oncology-based care, 53% and US$505.76, and (3) usual care, 25% and US$505.05. These results are based upon published US population demographics, pain management efficacy rates, and cost standards. The results will change based upon the tailored inputs.
Conclusion: A rational and comprehensive approach to cancer pain management will lead to improved pain control and lower resource use. This economic model can be used to assist health care decision-makers in advocating policies that include coordinated cancer pain management.

PP2. "THE COST OF RADIOTHERAPY FOR BONE METASTASES. A QUALITY ADJUSTED ANALYSIS"

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AIMS

To assess the cost of radiotherapy for bone metastases after adjusting for differences in response rate.

METHOD

The fixed and variable costs of delivering an average radiation field have previously been reported. The records of patients treated with radiotherapy for bone metastases were examined for treatment and outcome details. The total cost was calculated by multiplying the average number of fields by the cost per field. The average duration of survival was calculated. This value was modified by the average response of patients as reported in the literature. Partial response (PR) and complete response rates (CR) were pooled from the available published randomised controlled studies. A cost per response adjusted life year was then calculated. We tested the sensitivity of the cost per life year by varying the weighting for partial responses.

RESULTS

A radiotherapy field cost on average $69 AUS in 1991. Costs included capital, labour, consumables and overheads. 903 patients treated between July 1991 and July 1996 for bone metastases were examined. They received an average of 10.9 fields per treatment. The total cost for treating this population was $685,421. The average survival was 14.6 months. The effect of CR was weighted at 1 and PR at 0.5. From this an overall response rate was derived by adding the CR to the weighted PR. The median response rate was 58.5% (range 26.5% - 73.5%). The median cost per month was $89 with a minimum of $71 and a maximum of $196. The assumption that PR is worth 0.5 of CR was tested by varying PR rates from 0.0 to 0.9. This varied the overall response rate from 41% to 72.5% respectively and the cost from $127 per month to $72.

CONCLUSIONS

Radiotherapy for bone metastases is a relatively inexpensive and effective manoeuvre with the overall cost per life year being $1,067. It compares favourably with many other interventions in cancer medicine.

PP4. THE ECONOMIC EVALUATION OF A PORTFOLIO OF HEALTH CARE INVESTMENTS WITH TREATMENT SYNERGIES.

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Portfolio theory is central to the analysis of risk in many areas of economics and is now gaining interest in health economics. This paper aims to construct a theoretical framework to apply portfolio theory to the evaluation of health care programs using Cost Effectiveness Analysis (CEA). To do this, a number of modifications are needed. First, the method of reporting the results of a CEA needs to be modified. Second, portfolio theory needs to be expressed in terms of effects to an aggregated population. Finally, one needs to allow for the possibility of a synergy between investments in the portfolio.

The impact of two health care interventions is explored for individuals and the population as a whole. A general formula for modified portfolio theory is derived and is applied under varying assumptions about the correlation between individuals and 'exposure' to the two interventions. The paper concludes that whilst modified portfolio theory adds a theoretical foundation to health care evaluations, it may not be operational until correlation data between interventions is measured. Further, the question of uncertainty in health care evaluation needs to be resolved. The paper also concludes that a synergy may be present at the individual level but in large sample it may not be measurable.

PP5. RISK AND UNCERTAINTY IN THE EVALUATION OF HEALTH CARE PROGRAMS.

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The use of economic evaluation tools such as cost-effectiveness analysis and cost-utility analysis has long been established in health. However, it is uncertain if such tools are based upon rigorous economic principles. Furthermore, it is clear that the use of evaluation techniques for resource allocation may bias choice away from some potentially beneficial programs.

To combat both this uncertainty in theory and bias in allocation a number of health economists are turning to Financial Economics for new inspiration. A key example of this is the use of portfolio theory in the evaluation of a bundle of health investments. There are a number of hurdles that have to be overcome before portfolio theory can become operational in health economics. This paper focuses on the divide between risk and uncertainty. While these terms may sound synonymous, in economics they have vastly different meanings that have often baffled both economists and non-economists.

This paper outlines the recent literature on portfolio theory in health economics and illustrates its main theoretical prediction, that is, a portfolio of health investments will have a reduced variance compared to its components. The paper will then focus on the divide between risk and uncertainty. It will be concluded that an "uncertain" intervention will not be diversified in a portfolio of other interventions.

PP6. COMPARING THE RESULTS OF COST-EFFECTIVENESS ANALYSES CONDUCTED IN GERMANY (D) AND THE NETHERLANDS (NL) FOR ANTIBIOTIC PROPHYLAXIS IN SMALL CELL LUNG CANCER PATIENTS (SCLC)

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Background: The results of a cost-effectiveness analysis conducted in one country may not be generalizable to other countries where health care financing, patient management strategies and cultures are different.
Objective: To compare the results of cost-effectiveness analyses (CEAs) conducted in NL and D for patients with SCLC who participated in a phase III trial concerning the use of prophylactic antibiotics versus placebo to reduce the incidence of febrile leucopenia (FL) and infectious deaths.
Methods: The multicenter trial with a 2x2 factorial design initially involved randomizing SCLC patients to receive either standard dose CDE (cyclophosphamide, doxorubicin, etoposide) or intensified CDE (125% CDE and G-CSF). In addition, patients were then randomized to be given both oral roxithromycin 150mg and ciprofloxacin 750mg twice daily or placebo on days 4-13 of each cycle of chemotherapy. Medical resource utilization was documented prospectively during the trial which included 33 patients from NL and 49 patients from D representing 21% and 30% of the total sample respectively(n=161). The CEAs take the perspective of the health insurance systems in each country.
Results: The outcomes from the clinical trial showed a 40% decrease in the incidence of FL and a reduction in infectious deaths from 6% to 0% in patients taking antibiotics[1]. In DE, there was an average cost-saving of 35 Euros (95%CI:(-)1,713-2,263) in favor of giving prophylactic antibiotics which is not significant. However, the cost difference in NL was 2,705 Euros (95%CI:(-)810-5,948), demonstrating savings in favor of prophylactic antibiotics of nearly 45%.
Conclusion: Giving oral prophylactic antibiotics to SCLC patients undergoing chemotherapy is cost effective in both D and NL, although the magnitude of the cost differences vary. The reasons may be due to per diem hospitalization costs, which are difficult to compare between countries as they comprise different resources. Additionally there are differences in the patient populations, the financing mechanisms of the health care systems and patient management strategies.

This study was partly sponsored by Bayer B.V.

[1]Tjan-Heijnwen VCG et al. Reduction of chemotherapy induced febrile leucopenia by ciprofloxacin and roxithromycin in patients with small cell lung cancer

PP7. OVARIAN CANCER PATIENTS PREFER ORAL REGIMEN BECAUSE OF CONVENIENCE.

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Objective: The goal of this study was to examine patient's preferences and beliefs about the route of chemotherapy administration (oral versus parenteral) in recurrent ovarian cancer. Current treatment of advanced disease includes surgical debulking followed by chemotherapy with paclitaxel and platinum. Despite encouraging short-term results, most patients will ultimately develop recurrence. Second-line treatment of recurrent disease continues to play an important role in the care of this patient population. Quality of life and patient preferences have not been well studied in this setting. **Methods:** Patients who have received 1st line IV therapy answered an investigator-developed survey of preferences and beliefs regarding route of chemotherapy administration. Patients rated statements from 1 (strongly agree) to 5 (strongly disagree). The willingness to accept additional costs for oral chemotherapy was also surveyed. **Results:** Of 45 patients assessed, 60% stated a preference for oral chemotherapy, 36% preferred IV chemotherapy, and 4% had no preference. Interestingly, even patients stating a preference for IV therapy were willing to pay an average of $645 per cycle for oral chemotherapy. While oral preference patients were willing to pay $716 out-of-pocket per cycle of chemotherapy.

Patient Reported Preferences and Beliefs, 1=strongly agree 5=strongly disagree

Questions	Oral (n=27)	IV (n=16)	No Preference (n=2)	P-value
IV more effective	3.4	3.1	5.0	
Pills more effective	3.2*	4.1*	5.0	p=.03
IV at clinic convenient	2.4*	1.1*	1.0	p=.005
Pills convenient	1.0*	1.8*	1.0	p=.05
Prefer pills at home	2.1*	3.6*	3.0	p=.007
Worry about IV line started	2.7*	4.4*	5.0	p=.003
Worry over emesis with pills	3.0*	4.0*	3.0	p=.03

Discussion: Patients preferred to home treatment to clinic treatment and felt strongly that oral chemotherapy was more convenient. This study suggests that many patients with recurrent ovarian cancer value their time away from a clinical setting and prefer oral chemotherapy at home.

PP8. COST OF CHEMOTHERAPY-INDUCED NEUTROPENIA, THROMBOCYTOPENIA AND NEUROLOGIC TOXICITY.

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Objective: Chemotherapy-induced toxicities (CIT) may have a significant impact on overall healthcare costs, diminish patient functioning, and interfere with treatment plans. There is limited research on the *total* costs associated with CIT, including indirect costs. The objective of this naturalistic, observational study was to assess the cost and quality-of-life impact of CIT in women with gynecologic cancers. **Methods:** Women experiencing CIT, as graded by NCI Common Toxicity Criteria, completed bimonthly questionnaires that assessed utilization (e.g., hospitalization, labs, physician visits, phone calls, home visits, medication, medical devices, lost productivity, and paid caregiver time). Direct medical costs were based on hospital cost-accounting data and indirect (i.e., productivity loss) costs were based on modified Labor Force, Employment, and Earnings data for both patient and spouse. **Results:** The mean age for women in the study was 59.5 years with an average household income of $44,990. The time in the study for hematotoxicity groups was 6 months and 8 months for the neurotoxicity group. The three toxicity groups were comparable in age, race, education and disease stage. Table 1 presents the mean direct medical and indirect costs.

Table 1	Total Direct Medical	Total Indirect	Total Costs
Neurotoxicity (n=42)	$26,032 (mean=$620) (SD= $391)	$177,259 (mean= $4, 220/patient) (SD=$4,823)	$203,290 $4,840/patient
Neutropenia (n=26)	$196,189 (mean = $7,546) (SD=$7,295)	$99,689 (mean= $3,834/patient) (SD=$4,374)	$295,878 $11,380/patient
Thrombocytopenia (n=15)	$61,074 (mean= $4,072) (SD=$3,467)	$64,233 (mean= $4,282/patient) (SD=$4,113)	$125,307 $8,354/patient

Conclusions: Chemotherapy-induced toxicities have significant direct and indirect costs. Neurotoxicity has a disproportionate amount of indirect costs. While the hematotoxicity groups have significant amounts of both indirect costs and direct medical costs. Future research on the costs of CIT should include an assessment of the impact of indirect costs. This study suggests that more emphasis should be placed on the prevention of toxicities in standard chemotherapy regimens.

PP9. COST CONSIDERATIONS IN THE MANAGEMENT OF CLINICAL STAGE I NON-SEMINOMATOUS GERM CELL TUMOURS (NSGCT)

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Background : It is important to estimate the cost of equally efficient management options (surveillance, retroperitoneal lymph-node dissection [RPLND] and adjuvant chemotherapy) given the high curability of clinical stage I NSGCT.

Methods : We calculated the cost of the 3 possible treatment strategies for stage I-NSGCT after orchidectomy and the initial work-up using data in the literature for the choice of follow-up procedures and relapse rates. Treatment in the event of relapse is based on routine practice in our institution
1/ surveillance alone : assuming a 30-35 % rate of relapses that are treated with 3 cycles of BEP with 20% of these cases undergoing surgery for residual masses.

or 2/ immediate RPLND for all patients 30% of whom have positive lymph nodes. These patients are subsequently treated with 2 cycles of BEP in our institution. Among the 70% with negative nodes, 7-12 % will develop an extra-abdominal relapse usually treated with 3 cycles of BEP.

or 3/ adjuvant chemotherapy with 2 cycles of BEP.

Neither orchidectomy, nor initial work-up (identical for all patients), nor second line salvage treatment (a rare event equally balanced across groups) were taken into account.
Costs are those applied at the Institut Gustave-Roussy and reimbursed by the National Health Scheme in France for 100 patients over 5 years for each group :

- surveillance (1 636 601 Euros)
- RPLND (1 447 984 Euros)
- adjuvant chemotherapy (1 850 613 Euros)

Conclusion : Although RPLND is the least expensive of the three options, there is no drastic difference in the overall cost of each strategy. Future research should therefore focus on quality of life and the evaluation of immediate morbidity and late toxicities for each option

PP10. WILLINGNESS TO PAY FOR SUPPORTIVE CANCER CARE: AN ECONOMIC POINT OF VIEW FOR HEALTH DELIVERY AND A POSSIBLE INDICATOR FOR PATIENT QUALITY OF LIFE.

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Cost-benefit analysis measures health interventions from social perspective. Willingness to pay (WTP) for a health benefit takes many aspects into account such as feelings towards medical intervention and how it meets cancer patient's quality of life (QoL) expectations. WTP analysis about supportive care could help to understand the need to improve patient QoL.

We performed it in 70 patients receiving cisplatin, informing them about the incidence of acute and delayed emesis (30% and 40%), risks of anemia following chemotherapy, transfusion incidence without (45%) and with prompt erythropoetin use (25%), transfusional HIV/HCV risks. The patients, 35 from urban and remaining from rural area, were asked their maximum WTP **1)** to reduce the risk of acute and delayed emesis to 20 and 30% **2)** to reduce the risk of anemia requiring transfusions support from 45% to 25% **3)** to have erythropoetin administered promptly during chemotherapy. We also asked their willingness to cover the costs of 3 months therapy with erythropetin (3000 $).

Urban pts had significantly higher annual incomes (<$19.000: 17% vs 50%, >$50.000: 17% vs 7%, p<.01), higher WTP for reducing acute (20%: $47 vs $17, 30%: $63 vs $25, p<.0001) and delayed risk emesis (30%: $40 vs $18, 40%: $51 vs $25, p <.0001). Between groups, there were no significant differences in WTP ($600 vs $540) for erythropoetin and the willingness to completely cover drug costs (31% vs 36%). In contrast 100% of pts with incomes >$50.000 but only 36% and 16% with incomes <$50.000 and <$19.000 were willing to cover erythropoetin costs.

Tax-funded health care systems have a higher prevalence of WTP compared with that found by Ortega et al. (Cancer 1998). Higher incomes in urban settings and different ways of life are associated with a greater WTP to prevent emesis. Aversion/fear of transfusions or poor disease knowledge can overcome income limits. From patient's perspective, our supportive care must be improved. In addition, different ways of life and cultural variations can interfere with supportive care feelings elicited by patients.

PP11. CLINICAL COURSE AND COSTS OF GLIOMAS IN FRANCE

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Glioma is the most frequent brain tumour. In France, incidence rate of malignant astrocytomas (glioma grade III and IV from WHO classification) is estimated at 2.38/100,000 per year. This rate increases both for men and women. No data have been published on costs and clinical management of gliomas in France.
Objective: To describe clinical course and resources utilisation of treated patients with malignant glioma and to estimate associated direct costs.
Material and methods: A retrospective data collection on procedures and resources consumed for glioma's treatment was performed from hospital medical files of patients after their death due to glioma. Costing of identified resources was performed using a standard costs approach with the perspective of the French Sickness Funds because these patients are fully reimbursed.
Results: 27 patients' files were analysed. Mean survival is 206 days from diagnosis. First-line treatment is always a biopsy associated with surgical resection for 41% of patients. Chemotherapy (63%) and/ or radiotherapy (55%) are used in addition to biopsy. Only 41% of patients experienced relapse. Second-line treatment is based on chemotherapy and concerns only a few patients (19%). For terminal care, 90% of patients are staying in an hospital close from their family or treated in an ambulatory setting. Main medical resources are consumed during short-term hospitalisations (63%). Day-care hospitalisations (especially for radiotherapy) represents a large part of resources used (20%). Mean direct costs to treat a patient suffering from glioma from diagnosis to death is estimated at 130,000 French Francs.
Conclusion: Medical management of patients with high-grade astrocytoma is not consensual and consumed important part of health care resources.

PP12. RADIOBIOLOGICALLY –BASED ASSESSMENTS OF THE NET COSTS OF FRACTIONATED RADIOTHERAPY.

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External beam radiotherapy remains one of the prime methods for treating cancer and radiobiological research has demonstrated that there is scope for improving radiotherapy outcomes. This may, for example, be effected through the use of altered fractionation (the dose-time pattern of radiation delivery), which can be optimised to suit the radiobiological characteristics of individual tumours. Optimised fractionation may require extended-day operation of radiotherapy departments and the institution of weekend working, measures which significantly increase the treatment costs. However, such short-term cost pressures need to be balanced against the longer-term cost-gains associated with improved tumour control.

For any particular type of fractionation the probabilities of curing the tumour and of inducing long-term normal tissue damage may be quantified using mathematical models which make use of intrinsic radiobiological parameters. By extending the models it is possible to include the costs associated with:

i) delivering more complex (tailored) fractionation,
ii) surgical (or other) salvaging of a failed primary treatment, and
iii) continuing care arising from impaired quality of life.

Thus it is possible to identify "cost-optimised" radiotherapy treatments. Whereas radiobiologically-optimised solutions identify the (theoretically) best possible treatment, irrespective of cost and practicality, cost-optimised solutions are additionally dependent on the balance between the initial cost of providing a complex treatment and the premium which is placed on avoiding clinical relapse or complications. The exact form of a cost-optimised radiotherapy treatment will thus depend on the prevailing health care culture.

The model has demonstrated the conditions under which complex fractionation treatments can be justified in terms of overall cost-effectiveness and is capable of identifying the tumour groups which cannot properly be treated by standard fractionation. Such models may be of significant value in providing quantitative arguments to support the case for improving the resources which are allocated to Radiotherapy Centres.

PP13. A MULTINATIONAL STUDY TO MEASURE THE VALUE THAT CANCER PATIENTS PLACE ON IMPROVED EMESIS CONTROL FOLLOWING CISPLATIN CHEMOTHERAPY

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One of the most significant breakthroughs this decade has been the 5-HT3 receptor antiemetics. Following their adoption, the control of acute emesis after cisplatin increased to approximately 70%. However, despite their use beyond the first 24 hours, up to 50% of patients still suffer from delayed emesis. The NK1 receptor antagonist are a new class of agents designed to reduce the risk of acute and particularly delayed emesis. Early data from double blind randomized trials suggests that an orally administered NK1 receptor antagonist can reduce the risk of acute and delayed emesis following cisplatin by 20% and 30% respectively (Navarri et al 1999).
To measure the value that cancer patients place on improved emesis control and quality of life, a willingness-to-pay (WTP) analysis was conducted in 230 cancer patients from Canada, Italy, Spain and Greece. After background information was presented, patients were asked the maximum that they would pay per day for a drug that reduced their risk of acute and delayed emesis (up to day 5) by 20% and 30% respectively. Using the payment card method to avoid starting point bias, patients where presented with WTP values starting from $0 up to a very high amounts.
To reduce the risk of acute emesis to 20%, Canadian, Italian and Spanish cancer patients were willing to pay $U.S. 40.00, $U.S. 24.00 and $U.S. 54.00 per day compared to $U.S. 6.00 from Greek patients (P<0.001). In the case of a reduction in the risk of delayed emesis to 30%, Canadian, Italian and Spanish cancer patients were also willing to pay per day for four days more than their Greek counterparts ($U.S. 32.00 vs $U.S. 17.00 vs $U.S. 39.00 vs $U.S. 5.00, P<0.001). These significant differences in patient value between countries remained, even after adjusting for socioeconomic variables (household incomes, children in the family) and previous history of emesis.
These results suggest that there are substantial cultural differences in how cancer patients value benefit and improved quality of life. Since the majority of the world's population resides outside of North America and Western Europe , there is a need to reevaluate our perceived level of patient benefit and measures of quality of life.

PP14. ECONOMIC EVALUATION OF THE RESOURCES USED BY PATIENTS WITH LUNG CANCER FROM THE TIME OF FIRST RECURRENCE TO THE TIME OF DEATH

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Background
The development of innovative and expensive treatments after failure of first-line chemotherapy requires data on how these new treatments will compare to existing strategies in terms of both medical results and costs. We conducted a cost analysis of the treatments of recurrence of lung cancer (both small cell-SCLC- and non small cell-NSCLC-) in France.
Material and methods
The study was a retrospective abstraction of patients' charts, consecutively drawn from three types of institutions: public, cancer centre, private for profit. All healthcare resources used from the diagnosis of first recurrence until the time of death were retrieved. Resources were monetized using the institutions ledgers, supplemented by the current reimbursement schedule for ambulatory care.
Results
Data on resource use was retrieved for 91 patients, 20 patients had SCLC and 71 NSCLC. Median survival after recurrence was 3 months for SCLC and 6 months for NSCLC
The diagnosis of recurrence, cost on average 600 Euros (total outpatient day, 400 Euros for tests alone) . Eighteen (25%) patients with NSCLC underwent surgery at an average cost of 6,000 Euro per patient. Radiotherapy was undertaken in 50 patients (39 NSCLC and 11 SCLC) at an estimated cost of 1,400 Euros per patient (1-2 courses). Up to seven lines of chemotherapy were used from the time of recurrence to the time of death for patients with NSCLC, two line for patients with SCLC. The average cost per line ranged from 1,200-3,400 Euros and increased over time. Palliation therapy was used in all patients, the average cost of follow-up, from the end of chemotherapy to the time of death was 14,000 Euros per patient.
Implications
When these results were compared with those of other European countries, we found that variations concerned mostly the use of chemotherapy. Whether these variations result from interpretation medical evidence, cultural differences or financial constraints remains to be determined.

PP15. REPRESENTING UNCERTAINTY IN ECONOMIC EVALUATION: THE ROLE OF COST-EFFECTIVENESS ACCEPTABILITY CURVES

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Decision making in health care is inevitably undertaken in a context of uncertainty concerning the effectiveness and resource costs of health care interventions and programmes. Therefore, two sets of related decisions need to be taken: those concerning appropriate service provision on the basis of existing information; and those concerned with whether to fund additional research to reduce the uncertainty relating to the decision. The decision concerning efficient service provision involves identifying the strategy associated with the best payoff given existing information, in terms of incremental cost-effectiveness ratios or net benefits. The decision concerning funding the collection of further information to inform service provision in the future involves analysing the uncertainty surrounding the decision.

Recently the technique of cost-effectiveness acceptability curves has been introduced; discussed and employed as a method to represent uncertainty within economic evaluation of health care interventions. The technique has benefits over confidence interval estimation for incremental cost-effectiveness ratios (ICERs), specifically avoiding the problems associated with negative ICERs and directly addressing the decision-making problem.

We present the concept of a cost-effectiveness acceptability frontier, which illustrates the uncertainty associated with the efficient service provision decision over the range of values for the pre-defined ceiling ratio (). The frontier addresses two limitations with existing examples of cost-effectiveness acceptability curves: the fact that they relate only to two treatment options; and the difficulty in their interpretation when the net benefit distribution is asymmetrical which is frequently the case in decision analytic modelling. The frontier is illustrated using examples from several clinical areas. It is concluded that cost-effectiveness acceptability curves represent a major move forward in how data from cost-effectiveness studies are communicated and interpreted by decision makers.

PP16. MEDICAL RESOURCE UTILIZATION AND COSTS OF DISTINCT EPISODES OF COLON CANCER

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Colon cancer is the second most frequently diagnosed malignancy in the United States, and the second most common cause of cancer death; however, little information exists concerning expected utilization and costs associated with possible outcomes that may occur after initial diagnosis (e.g., local recurrence). Victims of colon cancer may experience a range of outcomes, from complete recovery to distant metastasis and death. To date, utilization and costs associated with each distinct outcome remain largely unknown. This lack of detailed information hinders our ability to conduct cost-effectiveness studies of new treatments for colon cancer. This analysis addresses the gap in the literature by using linked cancer registry and claims data to estimate distinct episodes of colon cancer utilization and costs for several possible outcomes.

We focus on elderly patients identified in America's National Institute of Health cancer registry that have an initial diagnosis of colon cancer (post-1980) and claims in America's Medicare databases. Because Medicare covers much of the elderly U.S. population, it is particularly well suited for this analysis. We analyze claims information from 1991 to 1998. Because Medicare reimbursement levels are pre-determined based on reimbursement formulas, they are an excellent proxy for actual health care costs.

Episodes are ideal for evaluating cancer progression, because they group all claims associated with a particular illness, regardless of where or when the treatment occurs. For this analysis, we create two classes of episodes; one includes all colon cancer related care, the other includes all non-cancer treatment. We rely on the procedure and diagnosis codes contained in the claims data to evaluate whether each claim is cancer related. To identify end-points associated with specific outcomes, we look for certain pre-defined periods of inactivity in the claims data that suggest the individual is no longer seeking treatment for the cancer. Once the episodes are created, we use the resulting data to present summary statistics associated with each distinct episode.

PP17. PHARMACO-ECONOMIC COMPARATIVE EVALUATION BETWEEN COMBINATION CHRONOTHERAPY OR STANDARD CHEMOTHERAPY FOR COLORECTAL CANCER.

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Pharmaco-economic assessments were performed taken into account the available data of 2 consecutive randomised trials performed by European Chronotherapy Group, comparing, in advanced colorectal cancer, an associative chemotherapy comprising 5 FU, folinic acid, and oxaliplatin given either by flat or chronomodulated (with peaks at the times of least toxicities of drugs) infusions JNCI 1994, 86, 1608; Lancet 1997, 350, 681; ASCO 2000 : submitted). All patients were treated in ambulatory convenience.
We can summarise the results of these trials as follows :
1- In the chrono-arm, patients experienced 5 times less grades III-IV mucositis toxicity, 2 times less peripheral neuropathy and had to be hospitalised 3 times less.
2- In the chrono-arm, due to the better tolerance of the protocol, patients received higher overall drugs doses-intensities for both 5 FU and oxaliplatin.
3- Finally a higher response rate was observed in the chrono-arm (51 % vs 30 % in the flat arm) while progression free survival was also improved (10.6 months vs 7.5 m).

Taking those data into account, we evaluated the comparative total cost (in BEF) for both arms of the randomisation, and then the cost for every patient and course. These economic assessments were derived from the cost for each stay in day-hospital (or in classical hospitalisation, ie, for complications) with regard to lump sums or estimated mean daily cost, cost of medications knowing median doses of chemotherapy per course and the number of courses (569 in flat vs 732 in chrono arm), cost of ambulatory pumps (for programmation, redemption according to initial cost at selling,...), cost of disposable material (syringes, ramps, prolongators, modules, pouches,...), cost of medical (fees, honorarium) and paramedical (nursing, programming; cost per hour) staffs.

Finally, the evaluation could compare the relative cost according to the type of devices used (Intelliject vs Melodie pumps).

	FLAT 569 courses / 93 cases		CHRONO 732 courses / 93 cases	
	Intelliject	Melodie	Intelliject	Melodie
TOTAL COST	74.732.778	60.983.256	98.940.277	81.251.961
Cost/patient	803.578	655.124	1.063.874	873.677
Cost/course	131.340	107.176	134.868	110.592

The results (table) showed an equivalent cost for flat vs chrono arm by a reciprocal balance between
a- The costs of chemotherapy (higher in chrono-arm due to the higher dose-intensities, higher number of courses : in BEF 66.076.450 vs 45.554.250; also higher costs for day hospitals : BEF 30.265.418 vs 23.525.986 with the use of Intelliject pumps) and for oncologists (BEF 1.338.098 vs 1.040.832) and
b- The costs of complications (higher in flat arm ; BEF 377.981 vs 23.411) and of hospitalisations (BEF 3 .834.390 vs 1.235.905).

Therefore, we conclude to an evident cost-effectiveness in favour of the chrono arm, which appeared more active, less toxic and cost-equivalent. Moreover, with the implementation of the new devices, the Melodie pumps, an overall reduction of 18 % of global costs could be observed through the lower costs of the pump (ie redemption, disposable material, programmation,...) and the increased autonomy allowed for patients.

PP18. MEASUREMENT OF NURSING WORKLOAD IN CLINICAL CANCER TRIALS.

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In 1974 the EORTC Data Center was established: during their first year data was processed from 735 patients. In 1998, 6594 new patients were included in 157 ongoing studies, and 48 new studies were opened.

The present trend in chemotherapy treatment is to increase the dose of cytostatic drugs by using:

a) highdose chemotherapy plus peripheral blood stem cell transfusions
b) dose intensification schemes together with haematogenic growth factors and supportive care
c) chemoprotective agents

Another new development is the use of angiogenesis inhibitors with or without chemotherapy. With each new study the number of protocol requirements and supportive care needed results in more complex protocols. Potential acute and delayed side effects increases. Implementation of Good Clinical Practice, including monitoring all documents, is time consuming. A literature study shows that there has been little research conducted to determine and measure workload of nurses / datamanagers involved in clinical research.
In 1990-91 the EORTC ONSG conducted a survey to document nursing involvement in clinical cancer trials. Based on the results, guidelines for writing nursing summaries were established.
Nurses are now writing and implementing nursing protocols based on these nursing summaries to standardise treatment and nursing care resulting in more efficient planning and time allocation
This survey will be repeated to determine the changes in the involvement and workload of nurses during the last ten years and to determine which additional tasks have been added to their role. Tools will be developed to identify additional workload in an attempt to determine additional costs involved and staff requirements per study, according to the complexity of the study involved.

PP19. THE IMPACT OF SCREENING UNIT SIZE ON THE EFFICIENT PROVISION OF BREAST CANCER SCREENING IN THE UK

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Background
The UK breast screening programme (UK BSP), now in its eleventh year, is organised into a large number of individual screening units. Decision makers need to ensure that these units are producing efficiently, particularly as the programme is anticipated to expand.

Methods
Data envelopment analysis (DEA) was applied to investigate: the relative efficiency of UK breast screening units; the impact of screening unit size on efficiency; and how individual units could improve. The DEA model was developed using a series of specification tests so that it reflected the true characterisation of the production process. Sixty-four breast screening units were categorised into 33 large units (eligible population of >50,000) and 31 small units (eligible population of <50,000). Data were collected from these units using a national survey and KC-62 returns.

Results
Overall median efficiency score was 83%, forty four units were inefficient. A wide variation in efficiency scores was observed. Large units had a median efficiency score of 100% and twelve units were inefficient. In comparison smaller units had a lower median efficiency score of 94% and twenty units were inefficient. This difference was statistically significant (Mann Whitney, p=0.044). 45% of large units and 24% of small units were operating at constant returns to scale. Target improvements were identified for each inefficient unit.

Discussion
As there is scope for individual units to improve some of the new demand could be met through more efficient use of current resources. Since both large and small units operate at variable returns to scale, the source of inefficiency may not necessarily relate to scale. It will be necessary for decision makers to examine the practices of individual screening units before determining feasible options for improving resource use. DEA can help to identify these feasible options.

PP20. QUALITY-ADJUSTED TIME WITHOUT SYMPTOMS OF DISEASE AND TOXICITY OF TREATMENT (Q-TWIST) IN PANCREATIC CANCER WITH EITHER ENILURACIL/FLUOROURACIL OR GEMCITABINE

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A new oral chemotherapy in development, eniluracil/fluorouracil, has been studied in a phase III trial (FUMA3007) randomising patients to either eniluracil/fluorouracil or gemcitabine. One hundred and sixty-five patients were randomised (86 gemcitabine, 79 eniluracil/fluorouracil) and included in the Q-TWiST analysis. Q-TWiST is a measure of patient benefit incorporating toxicity, disease progression and survival in a single endpoint by defining a number of health states, TOX: time with treatment toxicity, REL: time with disease progression and TWiST: time without toxicity or progression. The states TOX and REL are weighted to reflect relative value on a scale from 0 (worst) to 1 (best). TWiST is given full weight. Q-TWiST was determined as the weighted sum of the state durations. The time spent in each state is given in the table below.

	Chemotherapy		Difference	
State	Eniluracil/ Fluorouracil	Gemcitabine	EU/5FU-GEM	95% CI*
	Mean (weeks)	Mean (weeks)	Mean (weeks)	Mean (weeks)
TOX	9.7	12.4	-2.7	-7.4, 1.2
REL	12.9	9.8	3.1	-1.9, 7.4
TWiST	9.6	8.7	0.9	-3.0, 5.0

* Bootstrap technique
Means are restricted means with median follow-up 430 days

Regardless of the relative weightings no significant difference between treatments was observed (Q-TWiST ranged from 1.5 weeks in favour of gemcitabine to 3.5 weeks in favour of eniluracil/fluorouracil). Eniluracil/fluorouracil provided 2.7 weeks less treatment related toxicity and approximately 1 week longer without toxicity or signs of disease and a shorter period with disease progression (3.1 weeks). None of these values reached significance.

Differences between traditional clinical endpoints such as overall survival, duration of toxicity and time with disease progression, make it difficult for an individual to contribute to the choice of chemotherapy. Asking the patient to weight periods of time with treatment related toxicity and disease progression and incorporating these relative weights into the Q-TWiST analysis can help in evaluating individual treatment options.

PP21. METHODOLOGICAL ASPECTS OF A RETROSPECTIVE COST-EFFECTIVENESS-ANALYSIS OF STANDARD AND DOSE-ESCALATED CHEMOTHERAPY OF ADVANCED HODGKIN'S LYMPHOMA

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Introduction
In the HD9 trial of the German Hodgkin Lymphoma Study Group (GHSG, 409 participating centres), standard chemotherapy (arm 1: 4 cycles of COPP-ABVD, n=262) was compared to the dose-escalated BEACOPP regimen (arm 2, 8 cycles, n=403) for advanced Hodgkin's lymphoma. Arm 2 is clinically superior to arm 1 and was expected to be more expensive due to use of G-CSF and other cost factors.

Study design
The aim was to find out the incremental cost effectiveness. Freedom from treatment failure was used as benefit. Resource data were extracted from the GHSG's data base and hospital files.

Methodological issues
(1) 66% of in-patient days in arm 1 and 38% in arm 2 were missing. The participating centres were asked at the 1999 annual GHSG conference and later in writing and by telephone to track these data down. 74% responded. A reduction to 21% (arm 1) and 13% (arm 2) of missing data (MD) was achieved. The remaining MD are accounted for using sensitivity analyses.
(2) Outpatient cycles were calculated on the basis of key resources from GHSG data sheets. Remaining cost factors were extracted from cost data from the University of Cologne Medical Centre (UCMC). Personnel was costed directly. Material, building costs and administration were converted from hospital overhead by divisional costing.
(3) The per diem charge (PDC) of the oncological department was used as estimate.

Discussion and conclusion
(1) Procedures to reduce MD of in-patient days were successful and show that such data can be obtained at a late stage. The reliability of data gathered later is, however, impaired.
(2) The detailed calculation of an out-patient chemo cycle can be successfully performed.
(3) PDCs in theory reflect costs, but may be distorted, e.g. by interdepartmental subsidies. PDCs can only be estimates of costs and make sensitivity analyses necessary.

PP22. COMPARING ECONOMIC EVALUATION METHODS WITH NEW CHEMOTHERAPEUTIC REGIMENS.

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Evaluating cost and cost-effectiveness of newer therapies is an important goal that remains difficult to achieve. Barriers to frequent measurement of these parameters include the burden of the evaluation and a lack of consensus on the proper methodology. While prospective evaluation is considered to be the ideal approach, it is also the most difficult. The object of this report is to examine economic evaluations of the same chemotherapy combinations (Vinorelbine + Cisplatin and Paclitaxel + Carboplatin in lung cancer), whether conducted prospectively or as part of an economic model. We had previously reported on an economic model examining different chemotherapy regimens (PROC ASCO 1997). The model concentrates on factors likely to be affected by the choice of the regimen (costs of: chemotherapy, supportive care agents, personnel, facilities, drug administration, and management of adverse reactions). These results were compared with those recently presented by SWOG in their prospective evaluation of these same regimens (PROC ASCO 1999). We hypothesized that end of life costs would be similar with both regimens, as were response and survival findings. The economic model predicted that the cost differential between the two regimens (the Paclitaxel regimen being more costly) would be $17,700 (US). Similarly, the SWOG prospective evaluation noted a $17,000 (US) difference in cost between the regimens. We conclude that: 1) further testing of carefully planned economic models is warranted, and 2) if results continue to show nearly identical findings (in cost differential), economic modeling could be widely employed and could demonstrate easily the relative economic factors associated with treatments yielding similar therapeutic results.

PP23. AN ECONOMIC ANALYSIS OF ORAL ENILURACIL/FLUOROURACIL VERSUS GEMCITABINE FOR ADVANCED PANCREATIC CANCER IN CANADA

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BACKGROUND: Eniluracil is an effective inactivator of dihydropyrimidine dehydrogenase (DPD), the first enzyme in the degradative pathway of fluorouracil (5-fluorouracil; 5FU). An open-label, multicenter, randomised, phase III trial (FUMA3007) compared the effect of a 28-day oral regimen of eniluracil/fluorouracil to that of intravenous gemcitabine in 165 patients with advanced pancreatic cancer.
OBJECTIVE: To assess the direct costs of eniluracil/fluorouracil versus gemcitabine in patients with advanced pancreatic cancer.
METHODS: Following data were collected: physician fees, costs of treatment clinic (including nursing time to administer the agent), pharmacy (drug preparation), ancillaries, managing adverse events (including hospitalisations) and drug acquisition costs. Only those treatment-attributable complications were included that were statistically different between the two treatment arms. Costs of all resources were obtained either from Ottawa Regional Cancer Centre or published sources. Costs, reported from the third-party payer perspective, are expressed in 1999 Canadian dollars (C$1 = US$0.69).
RESULTS: The total direct cost per patient for eniluracil/fluorouracil and gemcitabine for physician fees were C$92 and C$108, for treatment clinic costs C$214 and C$913, for ancillaries C$70 and C$151, for pharmacy C$11 and C$138, and for adverse events / toxicity C$314 and C$397, respectively. Drug acquisition costs were C$4984 for gemcitabine. While the cost of eniluracil/fluorouracil has not been set, these results demonstrate that even if the cost of eniluracil/fluorouracil therapy is set equivalent to gemcitabine, the total costs for patients treated with eniluracil/fluorouracil would be lower compared to gemcitabine.
CONCLUSION: The lower costs of administration, monitoring, managing toxicities, and the relative simplicity of the oral eniluracil/fluorouracil regimen results in a significant impact on increasing operational efficiencies and facilitating cost reductions in the management of advanced pancreatic cancer. Indeed, at a cost-per-patient parity with gemcitabine, eniluracil/fluorouracil still results in overall savings from the payer's perspective in Canada.

PP24. QOL SURVEY OF POSTOPERATIVE RECTAL CANCER PATIENTS IN JAPAN

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Objective: Although the incidence rate of rectal cancer has been increasing in Japan, many postoperative cancer patients have survived with some disability for the rest of their lives. We attempted to investigate QOL of postoperative rectal cancer patients using the Japanese EuroQol instrument. Based on the survey response, we compared the QOL of postoperative rectal patients with and without stoma.
Method: 498 rectal cancer patients operated at St.Mariannna University Hospital between 1978 and 1997 were selected from the Kanagawa cancer registry. Of these patients, 177 surviving patients were the subjects of this study. We conducted a postal survey of these patients using the Japanese EuroQol instrument with an additional questionnaire, inquiring about present symptoms and hospital visits. The prevalence of any problems in five dimensions was compared using the χ^2 test. The utility scores calculated using both UK and Japanese tariffs were analyzed using the un-paired t-test.
Results: 139 patients responded to the questionnaire, 46 of whom were ostomates. The mean age of the subjects was 69.3±10.3 yrs for ostomates and 69.1±11.8 yrs for patients without stoma. The prevalence of any problems in all dimensions was 53.8% for ostometes and 52.0% for patients without stoma. Although the prevalence of any problems in all dimensions was not significantly different, pain/discomfort of ostomete was significantly higher (p=0.0259). The utility-score using the Japanese tariff was 0.878±0.159 for ostometes and 0.835±0.170 for patients without stoma, which was not significantly different(p=0.1796) and that using UK tariff was same result(p=0.3952). Additionally, the VAS score was not significantly different (p=0.6689).
Conclusion: Although the QOL of ostomates was nearly equal to that of patients without stoma, they have some problems concerning pain and discomfort. A support plan for ostomates is desirable to improve their QOL.

PP25. COSTS OF ADVERSE EVENTS OF CHOP, COP AND FLUDARABINE IN CANADA (CAN), GERMANY (D) AND ITALY (I)

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Background: There has been little research into the treatment costs associated with conventional haematologic drug regimens. Published economic evaluations focussed on the use of Growth Factors or the impact of Bone Marrow or Stem Cell Transplantation in this therapeutic area.
Objective: To examine the costs (3rd party payer perspective) of frequent adverse events (AE) resulting from the use of conventional chemotherapeutic regimens in haematology.
Methods: Case Record Forms were retrospectively completed by 89 haematologists/oncologists (CAN 50, D 20, I 19) from the medical records of patients with low-grade NHL. For each patient, data on one cycle of therapy was collected, resource utilisation assessed, unit costs were applied and the result was multiplied by 6 to estimate the costs for an average course of treatment. Data on 424 patients was collected. The number of patients drawn from each cycle was similar, with fewer patients from cycles 5 and $\geq$ 7 (7.8%/8%) and more from cycle 6 (20%).
Results: Most commonly observed AEs (particularly grade III/IV) for all treatments was neutropenia/fever/infection (NFI) followed by anemia. The mean cost per patient for the treatment of AEs was 3381 in Canada, 3230 in Italy and 2590 in Germany. For all regimens and countries NFI was the most expensive type of AE. Per patient/per episode costs for AE-treatment were:

	(n=) tot. pats.	NFI	Nausea / Vomiting	Anaemia	Thrombocytopenia	Other
CAN	173	2299 / 4371	134 / 407	38 / 88	311 / 1795	599 / 1817
I	152	1418 / 3169	1060 / 3662	353 / 920	314 / 993	75 / 674
D	99	1194 / 3194	359 / 1145	715 / 1913	157 / 742	165 / 585

Discussion: Costs for the management of AEs was an important cost driver in all countries. New treatment options that reduce or avoid AEs, particularly NFI, will lead to substantial savings in total treatment costs. This confirms UK-results demonstrating a reduction of mean per patient cost for AE-management to 179 with the use of a low-AE-treatment (Rituximab).
[1]Sweetenham et al, British Journal of Haematology, 1999, 106, 47-54

PP26. INTERNATIONAL ASSESSMENT OF COSTS OF DRUG DELIVERY ASSOCIATED WITH CHOP, COP, FLUDARABINE AND RITUXIMAB

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Background: Economic evaluations of conventional haematologic drug regimens are rare. Published evaluations have focussed on the use of Growth Factors or the impact of Bone Marrow or Stem Cell Transplantation in this therapeutic area.
Objective: To examine the costs (3rd party payer perspective) of drug delivery associated with the use of conventional chemotherapeutic regimens and Rituximab in haematology.
Methods: The mode of drug delivery (inpatient/outpatient) in one cycle of therapy was determined from patient records of 642 patients from Canada (CAN), Italy (I), Germany (D), United Kingdom (UK) and France (F). If no data were available (COP - CAN, I, F; Fludarabine – D) the inpatient/outpatient-split observed with CHOP in the respective country was used for calculation. The number of administrations necessary over 6 cycles was determined according to the protocol and multiplied with unit costs for inpatient and outpatient administration respectively. For Rituximab 1 inpatient and 3 outpatient administrations were assumed for a 4 week treatment course with the exception of Germany where 46% of administrations were considered to be inpatient administrations (figure found for CHOP). Costs for iv-infusions, patient examinations (1 per cycle) and routine lab tests (1 set per cycle) were included.
Results: Per patient costs for drug delivery were:

	(n=) tot. pats.	Fludarabine	CHOP	COP/CVP	Rituximab
CAN	173	4791	1806	1222	920
I	152	3518	496	432	351
D	99	5186	1212	1176	886
UK	162	3287	741	741	798
F	98	8229	4281	4281	2107

Discussion: Costs for Drug Delivery are a major factor (at least as great as drug acquisition costs) for total direct treatment costs of conventional chemotherapies. Therapeutic options that offer a shortened treatment duration and/or a simplified mode of administration like Rituximab are likely to be economically attractive.

PP27. SMOKING CESSATION EFFECTS ON LUNG CANCER: RESULTS OF THE HEALTH AND ECONOMIC CONSEQUENCES OF SMOKING MODEL

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Background: 80-90% of all deaths from lung cancer are smoking-related and account for a large proportion of healthcare expenditure worldwide. Here, we present the number of smoking-related lung cancer cases and deaths and direct healthcare expenditure in a cohort of smokers in France, Germany, Poland and the UK as predicted over a twenty-year period. Methods: Results were obtained from the Health and Economic Consequences of Smoking (HECOS) model, which utilises discrete difference equations to model smoking status and health changes. A user-friendly interface was constructed using Visual Basic with an Access database. The model was prepared for and reviewed by the *WHO European Partnership Project to Reduce Tobacco Dependence*. A key purpose of HECOS is to demonstrate the burden that smoking-related diseases place on healthcare systems, and to demonstrate the potential disease cases averted, life years saved and reduction in the smoking-related disease costs which result from successful smoking cessation programs. Results: The model estimates that after twenty years 216,000 people in the smoking cohort of these four countries will have lung cancer, with a cumulative mortality resulting in 1,314,000 lung cancer deaths. The estimated direct healthcare cost of treating smoking-related lung cancer will amount to 12.8 billion euro in these smokers. The model also shows that a smoking cessation intervention with an average efficacy of 4.4% costing 40.23 euro per quit attempt, would avert approximately 533 cases of lung cancer and 21,605 deaths and cost 2,589 euro per life year saved. Conclusion: The HECOS model, which can be accessed on <http://www.who.dk/adt/ecos/whoweb.asp>, shows that the economic burden of smoking attributable lung cancer is immense. For a relatively small initial outlay, smoking cessation interventions can result in health gains, which, in the long term, will reduce the health care burden for smoking-related diseases.

PP28. A COST ANALYSIS OF CAPECITABINE AND VINORELBINE IN TAXANE-FAILED METASTATIC BREAST CANCER

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Purpose: This analysis compared the expected costs of capecitabine (XELODA®) to vinorelbine (NAVELBINE®) regimens studied in taxane-failed metastatic breast cancer.
Methods: Capecitabine's expected costs were analyzed with those of standard vinorelbine, high-dose vinorelbine, and vinorelbine/cisplatin. Acquisition, preparation, dispensing, administration and monitoring costs were estimated for the cycle duration and averaged per cycle day. These items and overhead costs were extracted from published Canadian sources. The provincial health care system perspective was used. Duration of therapy was less than one year; no discounting was applied.
Results: Daily treatment costs for capecitabine were $45.30/d. The alternatives were all estimated to cost more: standard-dose vinorelbine alone at $49.15/d; high-dose vinorelbine (+GCSF) at $192.50/d and vinorelbine/cisplatin at $68.08/d. The analysis demonstrated that adoption causes a shift in costs from cancer centres to provincial formularies. When intravenous preparation and administration costs, laboratory tests and clinic overhead were included, all regimens of vinorelbine were more expensive than capecitabine. Physician service costs and adverse effect costs extend this difference. The results are sensitive to the frequency of clinic follow-up and physician monitoring. The results are sensitive to recovering costs associated with intravenous clinic visits, and to drug acquisition costs.
Limitations: Capecitabine's relative benefit in terms of tumour response, disease progression, patient preference and overall survival was not directly addressed in this model. Further, standard-dose single-agent vinorelbine has not been demonstrated to have a therapeutic benefit in taxane-failed patients, and may not be considered an evidence-based comparator.
Conclusions: The cost comparison demonstrated daily per patient savings of $3.85 (8%), realised in metastatic breast cancer chemotherapy when capecitabine replaces vinorelbine for taxane-failed breast cancer patients.

PP29. INFERRING EFFECTIVENESS FROM PRESCRIPTION CLAIM DATA: CAPECITABINE ADOPTION IN METASTATIC BREAST CANCER

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Objectives: To determine the response rate, dosage, and length of response realised in breast cancer patients with capecitabine reimbursement from private and public payers.
Methods: Capecitabine (Xeloda®) was approved for metastatic breast cancer in September 1998. Ontario Drug Benefit commenced coverage by prior authorisation while private payers adopted it without restriction. Provincial claims data for 12 months ending September 1999 for both public and private payers were compared to pivotal trial results. Response rate was the proportion of eligible patients continuing therapy beyond 3 cycles. Dose reductions used initial and subsequent claim sizes. Length of response was assessed for patients monitored at least 8 months.
Results: 201 patients received capecitabine (public 120, private 81), most aged 45-64 years (44% public >65). Patients received one cycle per prescription. 48% of eligible public claimants received 4+ cycles (53% of private) of therapy (pivotal trial 21% RR). Doses were reduced in 29% public claimants (36% private) versus 30% in clinical trials. Another 13% had dose *increases*. Time to progression (pivotal: 6.1 months) was evaluable in 25% of the sample. Six patients (50%) reached this threshold, where only 3 would have been expected.
Limitations: Differences between claim frequency and cycle length may underestimate response rates. Claims for therapy not consumed may overestimate compliance. Right censoring of the cohort may underestimate length of response.
Conclusions: Coverage type had no effect on drug use. Prescription claims data are consistent with the pivotal trial results for response, tolerability and disease progression, and suggest post-market effectiveness in breast cancer may be better than expected.

PP30. COST-MINIMIZATION ANALYSIS FOR THE USE OF 5HT$_3$-RECEPTOR ANTAGONISTS IN MODERATELY EMETOGENIC CHEMOTHERAPY. A PROSPECTIVE PHARMACOECONOMIC EVALUATION IN GERMAN HOSPITALS

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This prospective multicentre cost-minimisation analysis was designed to compare the direct costs associated with the use of granisetron, ondansetron and tropisetron for the management of chemotherapy-induced nausea and vomiting (CINV) in german hospitals. To reflect daily clinical practice clinical and cost related data were collected under postmarketing surveillance conditions. 170 breast cancer patients receiving moderate emetogenic chemotherapy were evaluated. Effectiveness of 5HT$_3$-antiemetic therapy was based on clinical response defined as number of episodes of vomiting and/or nausea experienced by a patient up to 5 days following chemotherapy application. Total costs associated with CINV management were quantified for each patient and comprise aquisition and administration cost of antiemetic drugs as well as subsequent costs for treatment failures or side-effects. Although statistical comparison of clinical data is not possible due to lack of randomization results indicated that the complete control of nausea and emesis under everyday conditions (acute/delayed emesis 66-96%/65-79%; acute/delayed nausea 52-80%/22-40%) was similar to literature. To prevent acute emesis and nausea 100% of the granisetron, 19% of the ondansetron and 90% of the tropisetron group received the antiemetic drug once, 0%/ 51%/10% twice and 0%/30%/0% three times daily, respectively. 76-86% were additional treated with corticosteroids, 5-20% with other antiemetics. 2-15% needed rescue medication. To prevent delayed emesis and nausea 39% of the granisetron 96% of the ondansetron and 74% of the tropisetron group prescribed 5HT$_3$- antagonists, 66%/8%/27% corticosteroids and 100%/58%/47% other antiemetics. Average total costs per patient were 67,6DM/141,8DM/86,5DM for a combined in-patient out-patient setting with total drugs provided by the hospital. This result was robust to variation in key assumptions concerning drug acquisition cost and hospital individual treatment behavior although total cost for granisetron and ondansetron would become lower if data sheets of the most expensive hospitals were rejected from analysis. In conclusion this is the first prospective pharmacoeconomic evaluation reflecting the clinical reality of CINV management in German hospitals using different 5HT$_3$-receptor antagonists. The economic benefit of granisetron mainly reflects better guideline adherence and outlines their high economic potential.

PP31. IRINOTECAN IN FIRST LINE TREATMENT OF METASTATIC COLORECTAL CANCER: IMPROVED SURVIVAL AND COST-EFFECTIVE COMPARED WITH INFUSIONAL 5 -FU

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This paper is based upon a study by Douillard et al. (In press), which took a multicentre, randomised, controlled open label study comparing irinotecan (Campto®) in combination with 5-fluorouracil (5-FU) and Folinic acid (FA) therapy with 5-FU/FA alone, in the setting of first line treatment for metastatic colorectal cancer. This paper relates these data to relevant costs within the UK and to evaluate the economic implications of the difference in survival between the two treatment arms. This cost-effectiveness analysis compares the economic implications of replacing 5-FU/FA therapy as a single agent (de Gramont regimen) with irinotecan in combination with 5-FU/FA (de Gramont regimen).Drug acquisition costs are derived from the British National Formulary (March 1999), unit costs for clinical consultations and services are derived from relevant 1997/1998 cost databases. Costs associated with treatment delivery and disease complications are also considered. Indirect costs although important are not included, in line with the viewpoint of commissioners within the National Health Service. Cumulative drug acquisition costs per patient are higher with irinotecan and 5-FU/FA in combination than with infusional 5-FU/FA therapy alone. These costs are at least partially offset by lower cumulative costs per patient associated with treatment of complications in the irinotecan and 5-FU/FA arm than in the 5-FU/FA alone arm.

The cost effectiveness ratio calculated is £14,794 per life year saved. Therefore, irinotecan, in combination with 5-FU/FA can be considered cost effective by commonly accepted criteria. A sensitivity analysis was conducted on the extent to which 2nd line chemotherapy was received by isolating the UK data. This analysis only altered the cost effectiveness ratio slightly to £16,015. The clinical and economic data show that irinotecan, in combination with 5-FU/FA in the first line setting (Douillard et al. in press) has a major role in the management of colorectal cancer.

PP32. WILLINGNESS TO PAY TO REDUCE RISK OF ENT CANCER IN SWITZERLAND

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Purpose: The authors apply the contingent valuation method (CV) to assess the value placed on a reduction of the risk of ENT cancer among a sample of the Swiss population. An ex-ante approach is adopted in order to value health as a private good. **Method**: In April 2000, a survey is carried out on a group of 150 individuals in the French region of Switzerland. Interviewees are asked to express their willingness-to-pay (WTP) to reduce their own risk of ENT cancer. Three pieces of information are communicated: risk factors, consequences of the disease on quality of life of patients and the average risk of contracting it by gender. The elicitation format is a payment card followed by a bidding game. A sensitivity analysis is conducted by randomly proposing a 50% or a 95% risk reduction. **Results**: Zero stated WTP are examined in order to identify the refusal to participate in the contingent market arising from strategic or ethical motivations. It is possible to identify them by questions on the reasons for refusal and by statistical data analysis – Logit and Probit models. The internal validity is checked by applying different models, e.g. the semi-logarithmic, Box-Cox and Heckman specifications. It allows to understand how individuals' characteristics influence WTP. For example, the impact of smoking status, drinking habits, age, gender and income are checked. **Conclusion**: Such an economic study provides an assessment of the monetary value placed on the health outcomes of ENT cancer. It may contribute to better understand the risk perception of the general population and to improve the prevention of ENT cancer.

PP33. TREATMENT RELATED MIGRATION PATTERNS OF RADICALLY TREATED PATIENTS WITH CARCINOMA OF THE PROSTATE: THE IMPACT OF RADIOTHERAPY RESOURCES WITHIN THE PROVINCE OF BRITISH COLUMBIA.

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Background: British Columbia (B.C.) is the third largest province in Canada with a male population of 2 000 000, an estimated number of new prostate cancer cases of 2700 patients per year and an age standardized incidence rate of 156 per 100 000. The British Columbia Cancer Agency (B.C.C.A.) is solely responsible for delivery of all radiotherapy services. From 1986 to 1998 an expansion in resources has doubled the number of provincial cancer centres and more than tripled the number of available radiation oncologists.
Objectives: To assess the effects of radiotherapy resources on migration patterns of radically treated prostate cancer patients in the province of B.C.
Methods: A retrospective review of the B.C.C.A database was conducted. All prostate cancer patients treated radically with radiotherapy (n=9049) from January 1986 to December 1998 inclusive were identified. A total of 8814 patients were available for analysis. Patients were identified by geographic region of diagnosis and region of treatment. Annual migration matrices were constructed.
Main Outcome Measures: Absolute number of migrants as well as interregional, in-migration and out-migration rates were calculated for each year. Changes in migration rates were assessed in reference to changes in available intra- and extraprovincial radiotherapy resources.
Results: A large change in Vancouver net migration rates occurred with the incorporation of extraprovincial resources (from 0 to –700/1000 patients treated) confirming the need for these services. Also, increasing radiotherapy resources led to a significant shift in interregional migration rates (from 24/1000 to 385/1000 patients treated).
Conclusion: Migration rates appeared to be significantly influenced by provincial radiotherapy resources. The patient net migration rate for a treatment catchment region may represent a measure of operational efficiency, and the interregional migration rate may be thought of as the efficiency of a provincially funded program. This example of patient mobilization may serve as a model for other expanding oncology programs.

PP34. ANALYSIS OF MEDICAL RESEARCH ARTICLES ON ECONOMIC ISSUES IN MALIGNANT DISEASE USING THE HEALTH ECONOMIC DATABASE (HEED)

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The number of medical research articles on economic issues in malignant disease has risen exponentionally in recent years. Using the commercially available Health Economic Database (HEED), our goals were to determine the number and quality of economic studies between 1975 and 1999. HEED contains, as of January 2000, approximately 18,500 references. The primary sources used are the following on-line databases: Medline, Embase, Health Planning and Administration, Psychinfo and DHSS-Data. Nearly half of the references have been reviewed according to a standard report format by an experienced health economist. We analysed a dataset of 1220 publications dedicated to malignant disease (ICD9: 140-208+284), 65% published in a peer-review journal. 985 (81%) publications were communicated since 1995. 679 publications originated from or were applicable to North America, as compared to 448 to Europe, 58 to Australia, 32 to Asia, and 30 to Germany in particular. 256 publications were considered or contained randomized, 641 observational studies. The rest were pure or combined meta-analyses, review articles, modelling or judgement. The type of economic evaluation was alone or in combination: cost consequences (n=536), cost effectiveness (n=477), cost analysis analysis (n=194), cost utility (n=134), cost minimisation (n=118), cost of illness (n=47) and cost benefit (n=25). Most of studies dealt with pharmaceuticals (n=474), screening (n=326), or issues termed surgical (n=308), diagnostic (n=174), care (n=162), prevention (n= 110), radiotherapy (n=78), education (n= 13) and smoking cessation (n=3). Nearly all publications included direct provider/purchaser costs (n=1183). Other costs analyzed referred to hospital (n=1000), patient (n=49) or non-health service public expenditures (n=19). The studies were wholy or partially sponsered by government/publicity (n=131), research council/university (n=104), pharmaceutical industry (n=80), charity (n=30), non-pharmaceutical industry (n=20), public health care institutions (n=19) and private health care institution (n=1). In 330 publications the sponsorship was not revealed. In conclusion, we considered HEED a useful tool for discreminationg between qualitatively high and low research articles on economic issues in malignant disease.

PP35. THE ECONOMIC EVALUATION OF CANCER CARE USING A SYSTEM MODEL

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Purposes: This is to clarify the present and future relationship between the input resources and economic effects of cancer care for developing evidence-based health policy, and to get the useful tool of the appropriate decision making and informed consent for improving patient services.
Methods: We developed a system model, similar to the Marcov Model, of prognosis of principal seven cancers and analyzed the balance of patient labor productivity (Benefit) and accumulated cancer care costs (Cost). We estimated the probability of the paths to follow any of the routes, and cancer care costs from screening to palliative care. Such complex factors as the age differences of progress of cancer have been accounted for to build a valid system model. We also simulated future changes of cost-benefit ratio, QALYs and potential years of life lost when the cancer prevalence or the 5-year survival rate would be improved.
Results: The cost-benefit ratio of male stomach cancer (1.34) is above 1, while the ratios of male lung (0.17), prostate (0.37), colon (0.64) and rectum (0.72) cancers are below 1. The ratios of lung, rectum and colon cancers for the age of forties are lower than sixties for both sex. This is because screening costs pile up due to low cancer detection rate in younger age. The costs per QALYs gradually increase as the age advances, and those of lung and rectum cancers are relatively high. If the death rate decreases for 1 %, the ratio of stomach cancer increases for 2.3%, and that of prostate cancer decreases for 2%. When the 5-year survival rate draws to 100%, the ratio of lung cancer remarkably increases, on the other hand that of stomach cancer and cervical cancer declines.

PP36. COST-UTILITY ANALYSIS OF VARIOUS TREATMENTS FOR NON-SMALL CELL CARCINOMA OF THE LUNG

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Purpose: This report outlines the results of a cost-utility analysis comparing various treatments for patients with non-small cell lung cancer (NSCLC) from Radiation Therapy Oncology Group (RTOG) protocols. This incremental cost-utility study compares hyperfractionated radiation therapy (HRT), induction chemotherapy and standard radiation therapy (ICT + SRT), induction chemotherapy, concurrent chemotherapy and standard radiation therapy (ICT + CCT +SRT), concurrent chemotherapy and hyperfractionated radiation therapy (CCT +HRT) to standard radiation therapy (SRT).
Methods & Materials: Quality adjusted survival was obtained from various treatment arms of RTOG protocols evaluating different treatments for NSCLC using Q-Time and Q-Twist methodology. Costs were calculated from a payor perspective, i.e. Medicare reimbursement. Cost was modeled based upon treatment, as detailed by protocol specifications. The Red Book average wholesale drug price was used to calculate drug costs.
Results: The incremental cost-utility in US$/Quality adjusted life (QALY) year as a function of quality adjusted survival method found ICT +SRT to be the most cost-effective treatment; $7,471.50 Dollars/QALY for Q-Time analysis and $18,590.55 Dollars/QALY for Q-Twist analysis. ICT + CCT+ SRT was not cost-effective in both analyses while CCT+HRT was cost-effective in the Q-Time analysis but not in the Q-Twist analysis.
Conclusion: Induction chemotherapy and standard radiation therapy appears to provide the most cost-effective treatment for patients with NSCLC and KPS of 90-100. The only treatment not within the "acceptable" cost-effective range in both analyses was ICT +CCT +SRT with CCT+HRT not being cost-effective in the Q-Twist analysis. This resulted because the increase in quality adjusted survival in this arm compared to standard radiation was not great enough to offset the increase in cost encountered by patients treated in this fashion. Cost-utility differed based on the methodology used to calculate quality-adjusted survival. The implications will be discussed.

PP37. ECONOMIC AND QTWIST ANALYSIS OF ADJUVANT TREATMENT OF MALIGNANT MELANOMA WITH INTERFERON ALFA-2a. (IFNα2a)

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We performed a medico-economic analysis of adjuvant therapy in malignant melanoma based on data of a clinical trial (489 eligible patients). In this randomised controlled trial either no therapy or 3 MU of IFNα2a was given 3x weekly for 18 months after resection of primary malignant melanoma (>1.5mm, no clinical evidence of lymph node metastasis).
Disease free survival (DFS) and Overall Survival (OS) were significantly improved. 10% of treated patients experienced grade II/IV toxicities.
We extrapolated survival and estimated total costs over 10 years (lifetime) of both strategies.
Literature, expert opinion and survival curves were used to estimate risk of relapse and death between end of follow up and 10 years (lifetime).
Resource utilisation was derived from the RCT, literature and expert opinion to ensure agreement with current clinical practice. They included the medical management of the strategies using the perspective of the French Sickness Funds

Principal results are presented in the following table:

Mean/patient	IFNα2a	Surgery	Difference
OS/5 years	4.45	4.19	0.26
OS/10 years (extrapolated)	7.87	7.20	0.67
OS/lifetime (extrapolated)	16.87	14.28	2.59
IFNα2a-costs	4,284		
Total costs (5 years) in €	11,478	7,735	3,743
Total costs (10 years) in €	18,936	14,491	4,445

Cost -efficacy ratio can then be estimated at 14,400 € per life-year-gained (LYG) at 5 years, 6,635 € per LYG at 10 years and 1,716 € per LYG for lifetime.
Adjuvant therapy after resection of primary malignant melanoma is a cost-effective medical intervention. Low dosage of IFNα2a and good tolerability resulting in low costs for the treatment of side effects contributed to this. Because of the low rate of side effects the QTWIST analysis showed that results were not disrupted (OS/10 years -7% or + 5 % according to the values for life with toxicity and relapse). Even the most conservative scenario assuming no real survival benefit and no further benefit in DFS after 5 years (drop-dead assumption) results in a cost per Qaly of 26.147 €. Costs per LYG of adj. treatment with IFNα2a is below widely used and accepted standard therapies (e.g. screening of blood donors for HIV, BMT for ANLL).

PP38. RADIATION ONCOLOGY IN DEVELOPING COUNTRIES - ASSESSING INTERVENTIONS IN TELETHERAPY, BRACHYTHERAPY AND PERSONNEL FOR MAXIMUM IMPACT

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A survey was undertaken of the radiotherapy infrastructure in 73 Member States of the International Atomic Energy Agency (IAEA) in five developing regions: Africa, Asia & Pacific, East Europe, South and Central America. Four countries included are considered to be developed according to World Bank classification .

A] Economic indicators and teletherapy

A useful relationship is demonstrated between log [Gross National Product (GNP)/Capita] and log [Megavoltage machines per million population] which reflects not only the capital investment but also the ability to sustain equipment in good order. Where equipment number is disproportionately high compared to GNP/Capita, the equipment is generally of poor quality and/or poorly maintained.

The relationship ceases to be useful when the available equipment approaches the national needs for cancer management seen in developed countries in the regions studied and North America and West Europe.

B] Brachytherapy capacity (brtx-cap) and cervical cancer

To determine the availability of brachytherapy for the management of cervical cancer, the most common cancer in many developing countries, all brachytherapy useful for this purpose was reduced to a single number, brtx-cap, by attributing a patient capacity to each type of equipment: manual afterloading (50/yr), remote LDR afterloading (80/yr) and HDR (500/yr). This correlated poorly with the cervical cancer incidence in the Asia & Pacific region and appeared to follow the economic indicators and thus megavoltage machines more closely.

C] Radiation oncologists

In the Asia and Pacific region, no correlation was found with economic indicators or general health care standards. The paucity of trained personnel was frequently the limiting factor in delivery of radiation therapy in the African and Asia & Pacific regions.

These data, available from IAEA, are useful in ascertaining economically achievable standards and identifying weak links in radiotherapy delivery for optimal intervention by governments and donor institutions.

PP39. HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH ADVANCED BLADDER CANCER TREATED WITH GEMCITABINE PLUS CISPLATIN VERSUS MVAC: RESULTS FROM A PHASE III CLINICAL TRIAL.

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Objective: To compare health-related quality of life (HRQoL) in patients with advanced bladder cancer treated with two chemotherapy regimens. Methods: HRQoL data were collected in a phase III, randomized, multinational trial comparing gemcitabine plus cisplatin (GC) to methotrexate, vinblastine, adriamycin, plus cisplatin (MVAC). The EORTC QLQ-C30 was self-administered at baseline, after each cycle, and 30 days after discontinuation from study. Baseline HRQoL data were compared using analysis of variance (ANOVA) and longitudinal data were compared using an exploratory growth curve model. **Results**: Efficacy results were similar between the treatment arms with overall survival hazard ratio of 1.04. GC therapy was associated with more thrombocytopenia and anemia, while MVAC therapy was associated with more neutropenia, infection, mucositis, and diarrhea. The median number of cycles of therapy was 6 for GC and 4 for MVAC. 195 (96.1%) of the GC-treated and 194 (96.0%) of the MVAC-treated patients completed ≥1 questionnaire. On-study compliance was 81.8% for GC and 80.2% for MVAC. Baseline HRQoL scores were not different between treatment arms, except in the diarrhea item. Although statistical differences were detected in all scales (p=0.0001), not all were clinically meaningful. Global QoL improved by 8 points (pts) for GC while it was unchanged for MVAC. Fatigue worsened by 5 pts for GC and 11 pts for MVAC. Nausea/vomiting worsened by 8 pts for GC and 13 pts for MVAC. Appetite loss improved by 16 pts for GC but worsened by 6 pts for MVAC. Constipation improved by 17 pts for GC and 12 pts for MVAC. For other scales, the differences in maximum changes between arms were <5 pts. Conclusion: This exploratory analysis of HRQoL data further supports the use of gemcitabine plus cisplatin in the treatment of advanced bladder cancer given its favorable risk-benefit profile.

PP40. AN ACTIVITY-BASED COSTING MODEL FOR RADIOTHERAPY.

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Due to ever increasing health care expenses, economic studies, comparing the cost of the analysed treatments to the additional health care effects they produce, gradually become an integrated part of many clinical trials.

Accurate cost data on radiotherapy treatments are a prerequisite in cost-evaluation studies of radiotherapy protocols. Since literature data on this topic are scarce, other solutions have been proposed. Aggregate cost calculations, e.g. based on accreditation norms, do not produce sufficiently precise costs to differentiate between specific types of radiation treatments. The use of charges as a proxy for economic cost, often done in literature, may also lead to incorrect conclusions because differences between costs and charges can be important. Indeed, reimbursement of radiotherapy, varying significantly among different countries, does not adequately reflect the costs of delivering a specific radiotherapy treatment. Ideally, the actual resource consumption should be used as a measure of cost in clinical trials.

Activity-Based Costing (ABC), a cost calculation method that allocates costs to the different products based on their activity consumption, may generate such accurate cost data. The benefit of ABC has been demonstrated in business for products that largely differ in complexity and for products with an important proportion of overhead costs. Because both of these reasons apply to radiotherapy, it seems ABC may be of use in cost calculation of radiotherapy.

An ABC- model, in development at one pilot site, will be tested in 3 other radiotherapy sites in order to ascertain the general applicability of the programme. The aim is to generate accurate cost data of radiotherapy products, to improve insight in the cost structure of the irradiation process and to support managerial decisions in radiotherapy departments.

The steps performed in developing such an ABC- cost calculation model for radiotherapy as well as some practical applications will be presented.

PP41. THE COST-EFFECTIVENESS OF AROMASIN ™ (Exemestane): A EUROPEAN PERSPECTIVE.

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Aromasin™ (Exemestane) is a new option available for the hormonal treatment of advanced breast cancer. The main features of Aromasin are the irreversible binding to aromatase enzyme receptors and demonstrated clinical activity in patients who failed other hormonal treatments as second and third line therapy. In a recently completed phase III randomized double blind multicentre clinical trial, Aromasin has shown comparable tumor reduction rates and overall success, but longer duration of overall success, time to tumor progression and survival with respect to Megestrol acetate in post-menopausal women with advanced breast cancer failing to or refractory to tamoxifen.

Based on an observational study of the cost of management of advanced breast cancer in seven European countries and the results from the above-mentioned phase III clinical trial, the cost-effectiveness of Aromasin was simulated.

Methods:

A model was constructed, based on and driven by data on survival from the clinical study, including costs for Exemestane, Megestrol and cost for other treatments. Data from the observational study was used to calculate a country-specific daily cost of other treatments. Life years gained was used as the measure of effectiveness. Simulations were performed for 1,080 days ("within trial analysis") and for a life time perspective, where survival after the end of the trial was assumed to be the same as the trend during follow up.

Results:

When running the model for 1,080 days, within trial analysis, the cost-effectiveness of Exemestane compared to Megestrol varied between about 5,000 Euro and 13,000 Euro per life year gained. In Germany it was significantly lower (1,353 Euro) due to a higher cost of Megestrol. The total expected cost-effectiveness (model running until no survivors left) spanned between 3,554 Euro (Belgium) and 9,091 Euro (the Netherlands). The estimated cost-per life year gained is well within limits generally considered cost-effective.

PP42. THE COST OF THE MANAGEMENT OF ADVANCED BREAST CANCER IN EUROPE AND AUSTRALIA.

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In order to assess the cost of the management of advanced breast cancer an observational study was carried out in seven European countries (Belgium, France, Germany, Italy, Spain, the Netherlands and the UK) plus Australia. The purpose of the study was to understand similarities or differences in clinical practices between countries and to reveal the major cost drivers. The observational study was also designed to populate a model for calculation of the cost-effectiveness of a new treatment for postmenopausal women with advanced breast cancer failing, or refractory to tamoxifen.

Methods:

A retrospective observational study in which itemized resource use was gathered from medical records in eight countries was performed. Costs were divided into nine main groups: chemotherapy, hormonal therapy, supportive care, radiotherapy, surgery, blood transfusions, diagnostic measures, inpatient and outpatient care. 75 patients from each country, surviving at least 3 years from remission, were randomly selected and included in the study.

Results:

Inpatient care, chemotherapy, hormonal therapy and diagnostic measures were the dominating contributors in all cases, although their respective size varied between the countries. In Australia inpatient care contributed with 60% of the expected cost, while chemotherapy dominated the scene in the UK and Italy. Diagnostic measures were the largest cost in Spain (33 %). The last year of life was the most cost intensive in all countries. Costs varied between countries, both due to variation in different resource use and variation in prices for different resources.

PP43. COST COMPARISON BETWEEN HOSPITAL AND HOME CHEMOTHERAPY: A PILOT STUDY

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Background

Nowadays, the financial pressure on hospitals is such that all possible ways of reducing costs without diminishing quality of care are investigated with great care. In this perspective we have compared the total cost of hospital and home chemotherapy.

Method

From October 1998 to February 2000, intensive chemotherapy patients living within 25 km from hospital and with family support, were selected to participate for the study. They received the first two courses in the hospital setting, and the following courses of the same chemotherapy at home.Total costs, including direct and indirect costs, were calculated by matching hospital accounts with detailed data specific of each patient for the treatment cycles included in the sample.

Results

Out of a cohort of 12 eligible patients, 7 were included in the study (4 women, 3 men, mean age 57 yr., range 30-71). Two suffered from small cell lung cancer and were treated by ICE, two from lymphoma treated by BEACOPP, two from sarcoma and treated by Ifosfamide-Adriamycine and last one from myeloma treated by VAD.

The average total cost per day are compared in the following table :

Cost components	Hospital cost (CHF mean ±SD)	Home cost (CHF mean ±SD)	Hospita./home ratio
Doctors	28±3	31±5	0.9
Nurses and patient-related clerks	313±21	94±14	3.3
Housekeeping and laundry	92±6	0	
Transportation	0	78±50	
Paraclinical exams	101±51	36±14	2.8
Drugs and disposables	361±137	369±156	1.0
Total direct costs	*895±178*	*608±147*	*1.5 (p<.0002)*
Overhead expenses*	403	0	
Average total cost per day	**1298±239**	**608±147**	**2.1**

*Overhead expenses, i.e. the indirect costs, include management, logistics, general support.

Conclusion

Home chemotherapy turned out to be cheaper than hospital treatment by 50%. Fifty-five percent of this mean cost difference was attributed to overhead costs while 35% to nursing costs, as part of the work done by the nurses at the hospital was taken over by the family at home. Transportation expenses were balanced with avoided hotel costs. At home, more anti-emetic drugs were administered, but on the other hand fewer paraclinical tests were performed.

Therefore, home chemotherapy seems to be a good alternative to hospital treatment in selected patients.

PP44. POTENTIAL RESOURCE SAVINGS FROM REDUCED RISK OF CHEMOTHERAPY HOSPITALIZATION ASSOCIATED WITH GEMTUZUMAB OZOGAMICIN (CMA-676), A NEW ANTIBODY-TARGETED CHEMOTHERAPY IN TREATMENT OF RELAPSED ACUTE MYELOID LEUKEMIA (AML)

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OBJECTIVE: Current treatment of relapsed AML typically requires lengthy hospitalization for continous-infusion daunorubicin/idarubicin (days 1-3) plus cytarabine (days 1-7). We applied a societal perspective to estimate resources associated with outpatient administration of gemtuzumab ozogamicin, a new antibody-targeted chemotherapy, for treatment of relapsed AML.

METHODS: We pooled data from three single-arm, multinational, clinical trials in 142 patients with AML in first relapse. Gemtuzumab was administered as two biweekly IV infusions (2 hours each) at 9mg/m^2, in investigator-determined settings. Outpatients were defined as ambulatory before and after each dose, i.e., not pre-hospitalized or admitted on day of administration. We identified (at $p<0.05$) predictors of administration setting using trinomial logit models. Median hospital days at ~ 8 weeks following first gemtuzumab administration were compared, across settings, using rank-order tests. Survival duration was compared using Kaplan-Meier methods. The proportion of outpatients was compared (Maentel-Haenszel test) with a synthesis of 12 clinical studies on current AML (including *de novo* AML) treatment-related hospitalizations, generating relative hospitalization risk and potential resource savings.

RESULTS: Of all patients, 38% (54/142) received the first gemtuzumab dose as outpatients; this was independently predicted by screening and baseline platelets over 50,000/μL and US (versus EU) treatment. About 24% (34/142) of patients received both doses as outpatients, with median 8.5 (0-66) hospital days, compared to median 30.5 (1-133) days for the remaining 108 patients ($p<0.0001$). Survival duration was similar (log-rank $p=0.82$). The combined outpatient chemotherapy rate in the 12 control studies was 1.1% (19/1,793), with median 14-40 hospital days. These data yielded a potential 23% reduction (RR=0.77, 95% CI, 0.70-0.84) in hospitalizations for AML chemotherapy and up to 7 fewer hospital days per patient associated with gemtuzumab.

CONCLUSION: Gemtuzumab ozogamicin is associated with reduced hospitalization risk for AML chemotherapy, with potentially cost-saving substitution of outpatient administration for hospital days for clinically suitable patients.

PP45. AN EXPLORATION OF THE COST-EFFECTIVENESS OF NEW CYTOLOGIC TECHNIQUES FOR CERVICAL CANCER SCREENING

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Objective To indicate what sensitivity, specificity and unit cost is required by new cytologic techniques for cervical cancer screening in order to be at least as cost-effective as conventional microscopy, and to compare the findings with published results.

Methods With the microsimulation programme MISCAN for the evaluation of screening policies we calculated the incremental number of pre-cancerous lesions detected, invasives prevented and life years gained, and the costs of medical treatment that are induced or saved when screening test sensitivity would be enhanced, for a five year interval screening programme between 30 and 60 years. Sensitivity of conventional microscopy is 80% for pre-invasives, 85% for micro-invasives and 90% for macro-invasives. Screening attendance is 80%. For different combinations of test sensitivity and specificity we calculated the extra costs of any new technique, at which it would be equally cost-effective as conventional microscopy.

Results Extra costs of a hypothetical cytologic technique for cervical cancer screening with 100% sensitivity and specificity for pre-cancerous lesions and invasive cancer should not exceed € 6.00 in order to be as cost-effective as conventional microscopy, and € 3.00 in case of a more feasible 90% sensitivity for pre-invasives. Higher or lower specificity has a minor influence on these amounts. These maximum amounts are higher in case of a higher background incidence, a less intensive screening schedule, and less screening attendance, and lower when the opposite occurs. Trials of new cytologic techniques report higher sensitivities than conventional microscopy, but they suffer from flaws in study design. Nevertheless, considered the extra costs even the most favourable results indicate a less favourable cost-effectiveness than conventional microscopy for all new technologies.

Conclusion When judged on their ability to improve cost-effectiveness of cervical cancer screening, neither of the new cytologic technologies that have been considered yet passes the test.

PP46. META-ANALYSIS OF RANDOMIZED STUDIES COMPARING THIRD GENERATION REGIMENS WITH CHOP IN PATIENTS WITH INTERMEDIATE OR HIGH GRADE NON-HODGKIN LYMPHOMA

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Background: In patients with intermediate or high grade non-Hodgkin lymphoma (NHL), third generation chemotherapy regimens have been introduced to improve survival in comparison with the standard CHOP regimen. However, most studies have found no difference between these two treatments. We conducted a meta-analysis to assess the effectiveness of third generation regimens as compared with CHOP.
Patients and methods: Our study included the randomized controlled trials published in English from 1970 to 1999. After a MEDLINE search, 5 trials were found to meet our inclusion criteria. A total of 1982 patients, that were enrolled in these trials, were included in the survival meta-analysis. Our methodology retrieved patient-level information from all of these subjects; survival up to 9 years after randomization was compared between the two treatment options.
Results: The results of our meta-analysis showed that, in comparison with CHOP, third generation chemotherapy did not prolong survival at levels of statistical significance (chi-square by log-rank test = 1.44, p = 0.23). The relative death risk for third generation regimens vs. CHOP was 0.92 (95%CI: 0.80 to 1.06; p=0.26).
Conclusions: We conclude that, on the basis of our meta-analysis, third generation regimens do not confer any survival benefit to patients with intermediate or high grade NHL as compared with CHOP.

PP47. USE OF MONTE CARLO SIMULATION MODELING TO ESTIMATE THE EFFECT OF ASPIRIN USE ON PROGRESSION OF COLORECTAL CANCER

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Improving our understanding of colorectal cancer is a high priority given the prevalence of the disease, the aging of the population, and the numerous opportunities for effective intervention. Biological and epidemiological evidence suggests that aspirin use may lower risk of colorectal cancer. To examine the cost-effectiveness of various aspirin use strategies, we constructed a model of colorectal cancer that incorporates the effect of aspirin. Because the effectiveness of aspirin use may depend upon the timing of use relative to the latent progression of the disease, we directly modeled the influence of aspirin on underlying stages of colorectal disease (including asymptomatic stages). To estimate the magnitude of aspirin's protective on the underlying stages of diseases, we used a novel combination of disease simulation and the observed relationship between duration of aspirin use and *diagnosed* cancer to infer knowledge about the effects of aspirin use on unobservable disease states. From the simulations, we find that aspirin is likely to work at multiple points in the disease process — both "early" in the disease by retarding polyp emergence and "late" in the disease by slowing transformation of a polyp into a malignancy. Our model suggests that aspirin use exerts a stronger influence earlier in the disease, a result that carries implications for the effectiveness (and cost-effectiveness) of aspirin as an chemopreventive intervention for colorectal cancer. From a methodological perspective, this study indicates that simulation modeling can play an important role in improving our understanding of disease and informing clinical and preventive guidelines.

PP48. ELICITING PATIENTS' PREFERENCES : DEVELOPMENT OF A DECISION BOARD IN ONCOLOGY

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INTRODUCTION
In developed countries, the physician-patient relationship is moving from a paternalistic model to new decision-making models that take patients' preferences into account.
OBJECTIVES
Our aim was to develop a Decision Board (DB) and to test its acceptability in a French Regional Cancer Centre regarding the decision on whether or not to use chemotherapy after surgery in postmenopausal women with breast cancer.
We present the development process for this instrument and report the pre-testing and test phases, as well as the corresponding results.
METHODS
A working group was created with oncologists, psychologists and economists. Following the first phase, i.e., the development process, a first version of the instrument was presented to health professionals. Their feedback led to important modifications of the instrument. The DB was then presented to experienced patients, which resulted in slight changes. The second phase consisted of pretesting the comprehension, internal and across-time consistency of the DB on healthy volunteers.
RESULTS
The DB was pre-tested in a group of 40 healthy volunteers. Eighteen respondents chose chemotherapy and 22 chose not to have chemotherapy. Comprehension rates were very high (≥87.5%). Internal consistency was assessed considering option attitudes based on outcomes and option attitudes based on process. Women always shifted their choices in a predictable way. Across-time consistency was appraised using the test-retest method with Visual Analog Scales. The Intraclass Correlation Coefficient was 0.97.
DISCUSSION-CONCLUSION
Due to cultural differences, the DB developed in our French Cancer Centre is quite different from the DBs previously developed elsewhere.
Our instrument showed good comprehension and consistency properties, which are corroborated by the DB literature.
Whether our DB is acceptable for patients with breast cancer is now tested. Patients' reactions will tell us which type of decision-making model is at work : is it the "shared decision-making model", the "patient as decision-maker" model, or the "physician as decision-maker" model?
Further research is needed in order to explore the shared decision-making process and clarify the concept.

PP49. TREATMENT PATHWAYS, RESOURCE USE AND COSTS IN THE MANAGEMENT OF SMALL CELL LUNG CANCER

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OBJECTIVE: Small cell lung cancer (SCLC) represents about 20% of primary lung tumours in the UK. The costs associated with the management of SCLC are significant, however few studies have been conducted in the UK to determine their true extent. The aim of this study was to obtain an estimate of the current patterns of treatment and associated resource use and costs for SCLC in the UK. METHODS: Study sites were two hospitals in Newcastle-upon-Tyne. A focus group meeting was conducted with local clinicians to clarify the expected pathways of SCLC care and to design forms for retrospective patient record data extraction. The forms were developed to capture resource use for the treatment phases: referral and diagnosis, active treatment, follow-up (pre-recurrence costs), retreatment(s), subsequent follow-up(s) and terminal care (post-recurrence costs). Data were collected on a consecutive series of 109 patients diagnosed with SCLC between 1994 and 1998. Unit costs were determined from a variety of sources including the Newcastle Hospitals NHS Trust Finance Department and the BNF. RESULTS: The total costs pre-recurrence significantly outweighed those post recurrence (£913,937, 73% vs. £345,816, 27%). Active therapy was the most resource use intensive phase in the pre-recurrence period constituting 48.5% of the total cost (£610,980). This was primarily due to outpatient visits and the long inpatient stays associated with chemotherapy (59% of this cost) and the high costs of chemotherapy agents and side-effect medications (36%). Similarly, diagnosis was costly (£220,457, 17.5% of total costs), predominantly due to outpatient visits associated with tests and investigations required to stage the disease and determine a management approach (63% of this cost) and the cost of these tests and investigation themselves (34%). In the post recurrence period, the majority of costs can be attributed to terminal care (£251,951, 20% of total cost) and the associated long periods of hospitalisation and/or hospice stays (82% of this cost). CONCLUSION: The results of this medical chart data analysis show that the costs of treating SCLC are considerable, although the variability between patients in terms of the type and quantity of resource use was very high. Such analyses provide a useful insight into resources used in actual clinical practice. This study has identified the major cost drivers and when combined with outcome data will form the basis of future economic evaluations of SCLC treatments.

PP50. HOW TO CHOSE A METHOD OF COST ASSESSMENT IN HOSPITALS AS A BASIS FOR STRATEGIC DECISIONS ?

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In the context of growing economic pressure in the french public health care system, we undertook a study of strategic decision-making based on the evaluation of the break-even point in a hospital unit. In the leukaphereses unit of the Leon-Berard Cancer Center we assessed the average effective cost and the average optimal cost for the health autorities and the marginal cost for the hospital's managers for one year (1997). We compared these costs with the ressources allocated to the hospital and examined the avantages and disavantages of the French Diagnosis Related Group (D.R.G.) system.

We defined a taxonomy of costs, relating direct, semidirect and indirect costs with variable and fixed costs. We estimated for one leukapheresis an average effective cost of 1938 USD, based on an annual activity of 323 leukaphereses, an average optimal cost of 1174 USD, based on a maximal yearly activity of 610 leukaphereses and a marginal cost of 730 USD. The differences in these estimates suggest that the leukaphereses unit has an over capacity, and so we calculated the break-even point. It reached a yearly activity of 957 leukaphereses. However, the yearly maximal production has been evaluated at 610 leukaphereses.

Therefore we propose that health autorities should encourage the centralisation of leukaphereses units to ensure economy of scale. They should also raise the value of the D.R.G. « ambulatory engraftment without operating act » which is currently only 719 USD. Also the hospital managers could decrease the fixed costs by reducing the capacity of the unit.

PP51. COMPARISON BETWEEN TWO DIFFERENT MOBILISATION REGIMENS FOR PATIENTS WITH BREAST CANCER UNDERGOING AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION: A RETROSPECTIVE COST-EFFECTIVENESS ANALYSIS

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Background: Cost analysis has become a significant aspect of many medical procedures. Peripheral blood stem cell (PBSC) transplantation has recently been object of economic evaluation in several countries including ours. Two distinct mobilisation therapies which include antineoplastic drugs are compared correlating their economic impact with the final amounts in PBSC harvests.
Design and Methods: From September 1996 to September 1999, 15 of 130 consecutive women affected of breast neoplasm in complete response were mobilised with two different chemotherapeutic protocols followed by subcutaneous G-CSF. Nine of them received epirubicin 120 mg/m^2 and cyclophosphamide 1g/m^2 IV plus G-CSF from day +5 until the end of PBSC collection (group A). The remaining 6 were given paclitaxel 200 mg/m^2 plus cyclophosphamide 3 g/m^2 IV followed by two distinct doses of G-CSF after the last PBSC collection (group B). The total cost of both procedures was calculated taking into account: drugs and hematopoietic factor prices, infusion equipments and nursery preparation and delivery expenses.
Results: Total cost calculated for group A and B was 1415.8 and 2791.3 euros respectively (increment of 50.7% for group B). Besides there was an additional expense in the second group for all them required at least one day of hospital admission, that implied 113,8 euros more. Refering to the PBSC collection, median count of MNC and CD34+ cells were 2.68*10^8/kg and 5.34*10^8/kg in Group A obtaining 3.76*10^8/kg and 3.78*10^6/kg for group B. All transplants were performed and no problems were observed in hematopoietic recovery.
Conclusion: Although more cases are needed, mobilisation regimens which include paclitaxel are more expensive than regimens including epirubicin/cyclophosphamide and only have a little benefit on mobilisation and posterior PBSC collection, independently of its potential antitumoral activity.

PP52. ECONOMIC IMPACT OF VALIDITY OF PROGNOSTIC FACTORS IN COLON CANCER WITH LIVER METASTASES. FIRST RESULTS OF THE "BEST CASES IN COLON CANCER (BCCC)" PROJECT[§].

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The prognosis of patients with liver metastases (LM) of colon cancer (CC) varies considerably. Therefore it is difficult to assess the survival benefit of various treatment modalities which differ considerably in the requested monetary resources. Most of these patients have a rather poor prognosis but there is a considerable fraction of patients surviving for more than 5 years. **Aim:** The aim of this study is to summarize the known prognostic factors for CC and for patients with LM of CC. Second, the validity of these factors is to assess by the methods of Evidence-Based Medicine (EBM). Possible clusters of prognostic factors will be identified and confirmed by testing indepen-dent patient samples. **Methods:** Experts in different fields were asked to present in a consensus meeting the known prognostic factors for CC in their disciplines, to estimate the relative importance of these factors and to provide the literature which confirms the validity of the named prognostic factors. The presented prognostic factors were compared with prognostic factors and the correspon-ding references listed in textbooks. The validity of the quoted references was analyzed by using the Methods of EBM. **Results:** The experts identified more than 150 factors which are expected to predict the prognosis of patients with CC. These factors were categorized in the dimensions of patients characteristics, characteristics of the tumor, therapeutic interventions, outcomes of therapy and exogenous factors (e.g. social environment). In the analysed textbooks we found only 2-3 prognostic factors for colon cancer but no prognostic factor for the subgroup of patients with LM. Most of the provided literature was not useful to confirm the prognostic validity of the identified factors. There are no known factors which predict the prognosis of patients with LM of CC. **Conclusions:** As the treatment of patients with LM of CC is associated with risks, side effects and costs it is essential to identify the prognosis of subgroups of patients. Unfortunately, the clinical significance of only few of the published prognostic factors has been confirmed. This study demon-strated that researchers are advised to check the validity of critical variables such as prognostic factors for survival which are the most powerful variables in economic analyses.

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PP53. ECONOMIC ASSESSMENT IN PATIENTS WITH ADVANCED LUNG CANCER.

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Introduction: In this study the quality of data records and the costs of care in both, small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) patients was investigated. The costs were analyzed according to six clinical phases of the disease.
Methods: Charts from 26 patients were analysed retrospectively. Ten patients were treated in a university hospital, 16 in a district hospital or a hospital for lung diseases. Indirect costs i.e. loss in productivity was not calculated. As measure for direct costs we used charges paid by social insurance and patients.
Results: In only 15 of 26 records a complete follow up from the first symptom to death was possible. Reasons for incomplete documentation were in in-patients: too many hospitals involved; insufficient identification of involved departments; inadequate quality of information transfer; missing follow up data; poor documentation of radiotherapy. Special problems with out-patients were incomplete documentation of number of consultations; incomplete description of lab tests, pain treatment records and management of side effects; no documentation of the terminal phase of disease in home care patients; no identification of doctor's qualification.
The total average costs per patient (SCLC and NSCLC, completed records only, n=15) were 17.512 Euro with 17.800 in SCLC and 16.676 in NSCLC. The average length of hospitalization was 46,8 days in SCLC and 42,4 in NSCLC. In SCLC patients the hospital cost were 88,0% of total costs and were 91,5% in NSCLC. Average cost of care in the university hospital was 22.030 Euro and was 11.520 in district hospital/lung hospital.
According to the phases of the disease we observed high costs in phase II (start of treatment) with 31% of total costs and in phase IV (second treatment) with 19%. These figures were well correlated with the costs of drugs and length of hospitalization. The costs of out-patients exceeded in no phase of the disease 10% of total costs.
Discussion: Possible consequences of this analysis are related to the quality of documentation in both in- and out-patients. Second, the largest difference in total average costs was seen in different types of hospitals. This difference may be justified by differences in quality of documentation or outcomes.

PP54. LOCAL ISSUES IN THE IMPLEMENTATION OF THE GYNAECOLOGICAL CANCER GUIDANCE

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The launch of the gynaecological cancer guidance "Improving Outcomes in Gynaecological Cancers" in July 1999 (NHS Executive) posed some issues about the local implications arising from its implementation. As the overall balance of the recommendations result in a more centralized configuration of cancer services, assessing the local issues that the guidance raises becomes quite important, given that regional pattern of access costs, management costs and outcomes vary significatively. The project was set up within the local context of the North Yorkshire Health Authority (NYHA). Because of evidence that there exist improved outcomes for patients treated by specialist multiprofessional teams, NYHA was interested in assessing local issues raised by the guidance.

The ovary, uterus and cervix are the fourth, fifth and sixth most common cancer sites after breast, lung and bowel in women in England and Wales. However, the average GP sees only one new patient about every five years. This low volume is thought to negatively affect the outcomes arising from the management of cancer patients. The first task of the project was to assess whether the national epidemiological variables: incidence rates, mortality and survival were replicated in North Yorkshire. Data about waiting time and frequency of GP attendances for the gynaecological cancers in the region was analysed as well. For this assessment, the data provided by cancer registries was used.

Second, an analysis of the current activity configuration of gynaecological cancer services in North Yorkshire was conducted. The data used was the Contract Minimum Dataset. This is designed to give the purchaser an activity summary of services delivered by a provider unit. The hospital data that are used to inform contracts are collected in the form of finished consultant episodes (FCEs). FCEs are defined as episodes where a patient has completed a period of care under a consultant and is either transferred to another consultant or is discharged.

Third, an analysis of the cost and outcome/benefits implications of the implementation of the guidelines concludes the project (although a number of issues are suitable for future research). A cost per FCE for each unit in NYHA region has been estimated and an estimate of the potential scale of shifts in costs following referrals from units to centres is provided. The potential benefits of the reconfiguration of the cancer services is assessed. The focus is placed on identifying the sources where the benefits (or disbenefits) are likely to arise from as a result of the implementation of the guidelines.

PP55. TREATMENT COSTS FOR ELDERLY AMERICAN WOMEN WITH BREAST CANCER

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Among American women, breast cancer is the most frequently diagnosed cancer and the second leading cause of cancer related deaths. Because of its high prevalence, breast cancer treatment is a major expense for the U.S. health care system. To date, no population-based studies have provided estimates of the cost for different treatment approaches for women with breast cancer in the U.S. Our study reports medical care costs for women diagnosed with breast cancer at age 65 or over between 1983 and 1996. Our database consisted of cancer registry data linked to insurance claims data , between 1990 and 1998, from the Medicare program, which covers nearly all U.S. citizens aged 65 and over. Total medical care costs are presented as well as cancer treatment costs, derived by matching cancer cases to a cancer-free comparison group and subtracting out baseline medical care costs. Cost estimates are presented by the phase of the cancer treatment-- during the initial treatment period, continuing care, and terminal care- and by age group, race, stage, and chemotherapy treatment. Costs are estimated for differing treatment modalities of mastectomy, breast conserving surgery (BCS) followed by radiation therapy (RT), and BCS only. For 31,858 women with early stage breast cancer undergoing BCS with RT, their monthly cancer treatment costs during the initial care period were significantly higher than for women undergoing modified radical mastectomy ($1844 vs $1398 USD). However, during the continuing care and terminal phases, no significant differences in treatment costs were observed between these two groups. Clinical trials have demonstrated comparable survival whether treated with MRM or BCS with RT for women with early stage breast cancer. This study will assess whether lifetime cancer treatment costs are comparable for these two treatment modalities as well.

PP56. ASSESSING FACTORS RELATED TO INSURANCE AND ACCESS THAT INFLUENCE EARLY STAGE BREAST CANCER TREATMENT PATTERNS INVOLVING ADJUVANT CHEMOTHERAPY.

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Recent clinical evidence has reported the beneficial effects of adjuvant chemotherapy in the treatment of all women diagnosed with early stage breast cancer (ESBC). (Osborne, 1998. Giguere, 1998) However, patients must decide whether the expected treatment benefits exceed the costs associated with treatment administration, monitoring and management of adverse events, as well as adverse quality-of-life implications associated with chemotherapy. Consequently, a large number of women may decide to exclude adjuvant chemotherapy from their treatment regimen. In Iowa, for example, only 27 percent of ESBC patients received chemotherapy between 1989-1995 based on Surveillance, Epidemiology, and End Results (SEER) cancer registry database. (Ritho, 1999)

It is crucial for policy-makers, concerned with high cost of treatment in cancer patients, to understand the factors influencing chemotherapy treatment patterns in the presence of treatment heterogeneity. (Piccat, 1997.) Preliminary results have shown treatment variation related to patient clinical, demographic, and insurance characteristics at the time of diagnosis.(Ritho, 2000) The purpose of this study is to determine whether factors associated with insurance status and access to providers influence adjuvant chemotherapy treatment patterns in Iowa. These factors include insurance categories such as Medicare, Medicaid, private insurance and per capita distribution of physicians by specialty across Iowa. We linked Iowa SEER patients diagnosed with ESBC between 1989-1994 to their respective hospital discharge abstracts (HCUP-3). (Brooks, *Medical Care*, under review.) A total of 6307 patients were identified with comprehensive information on insurance status. Logistic regression will be performed. Treatment rates across patient groups with similar access characteristics will be determined. The effect of high versus low access on therapy choices involving adjuvant chemotherapy based on insurance status will be discussed.

PP57. COST-EFFECTIVENESS ANALYSIS OF IRINOTECAN AS FIRST-LINE THERAPY IN ADVANCED COLORECTAL CANCER

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Background
It has been shown that the combination of irinotecan with fluorouracil is superior to fluorouracil alone in patients with advanced colorectal cancer as first-line therapy. In a recent randomised trial (Douillard et al., Lancet, 2000), median survival was 17.4 months for patients treated with irinotecan combined with fluorouracil as compared to 14.1 months in patients who received fluorouracil alone.
Objective
The objective of the study is to relate this statistically significant difference in overall survival to differences in costs of each alternative.
Methods
Medical care consumption data were collected prospectively as part of the trial that included 387 patients. A further retrospective data collection was designed to inform on further chemotherapy and disease cost after study treatment failure. The perspective for the calculation of cost was the French National Health System. Drug costs were assumed to be equal to public prices. Hospital costs were derived from French public DRG database. Consultation costs were abstracted from the the public tariff database. Censoring of medical care consumption data was handled using the method described by Lin et al. (Biometrics, 1997). Uncertainty will be explored through bootstrap analyses.
Results
The total costs including drug cost, cost of treatment administration, cost of the management of toxicites and cost of disease progression amounted to 182,000 FF (USD 26,500) per patient treated with irinotecan and 123,000 FF (USD 18,000) per patient treated with fluorouracil alone. When the difference in cost is related to the clinical benefit of irinotecan, the cost per life year saved amounted to 214,000 FF (USD 31,100). Uncertainly analyses are ongoing and results will be presented.
Conclusion
First-line therapy with irinotecan extends significantly survival, at a cost that remains within the limits currently accepted for new chemotherapeutic agents. Robustness of this conclusion to uncertainty is currently under investigation.

PP58. THE COST-EFFECTIVENESS OF G-CSF AND CHEMOTHERAPY TO MOBILISE PERIPHERAL BLOOD PROGENITOR CELLS

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Objectives – To establish the cost-effectiveness of two stimulation protocols that are currently used in the collection of progenitor cells from the peripheral blood circulation: G-CSF versus G-CSF and chemotherapy.
Setting – All patients admitted for autologous transplantation to the Institut Paoli-Calmettes, Regional Cancer Hospital at Marseille, France, between January 1993 and December 1997. Progenitor cells were primed by G-CSF and chemotherapy in 101 patients and by G-CSF alone in 178 patients.
Outcome measure – The number of CD34 cells collected from the peripheral blood circulation was retained as the measure of benefit since it is likely to determine the feasibility of clinical reinfusion and, ultimately, haematologic reconstitution.
Results - Patients who were subjected to a stimulation regimen consisting of G-CSF and chemotherapy reached a higher number of CD34 cells collected during fewer leukapheresis sessions at no extra cost. For each group the existence of a dose-dependent relationship between G-CSF and the number of CD34 cells collected was empirically validated. Neither stimulation by G-CSF and chemotherapy nor stimulation by G-CSF alone lead to economies or extra costs incurred during transplantation. The number of leukapheresis sessions, hospital length of stay due to chemotherapy and transplantation, number of platelet transfusions and the dose of G-CSF were found to be good explanatory factors of total cost variation.
Conclusion - Clinical and economic arguments were clearly in favour of the substitution of G-CSF and chemotherapy for the administration of G-CSF alone. The existence of a dose-dependent relationship between G-CSF and the number of CD34 cells provided new insight into the clinical effectiveness of this drug.

PP59. THE COMPARATIVE ECONOMIC VALUE OF RALTITREXED AND 5-FU PLUS LEUCOVORIN

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Colorectal cancer is the third most common cancer in Canada with approximately 16,500 new cases in 1999. Currently, 5-fluorouracil (5-FU) plus leucovorin is standard chemotherapeutic treatment. Raltitrexed, is a new class of cytotoxic drug. OBJECTIVE: To measure from a Canadian Ministry of Health perspective the economic value of raltitrexed 3 mg/m^2 once every three weeks and 425 mg/m^2 5-FU plus 20 mg/m^2 leucovorin for 5 days repeated every 28 days. Results of the study, a large North American trial, are reported elsewhere. In this abstract, results of Canadian patients are reported; specifically, cost per quality adjusted survival. METHODS: Quality adjustments were conducted by rewarding survival time without toxicities and disease progression while penalizing time with toxicities or disease progression. Healthcare costs by type of resource and economic perspective were collected from five centers that participated in the clinical trial in Quebec and Ontario. RESULTS: 103 patients were eligible for analyses, 50 in the 5-FU+LV group and 53 in the raltitrexed group. Without adjustment for quality versus quantity of survival, the median time to death from Kaplan Meier estimates were equivalent 496 and 493 days, respectively. Both time to progression and time with toxicities favored patients treated with raltitrexed. Thus, quality adjusted survival favored patients treated with raltitrexed, 269 versus 370 days at the median. Direct drug cost favored 5-FU+LV, $130 versus $1,005 for an average cost difference of $875; nonetheless, the incremental cost per QALY for raltitrexed was $3,159 (95%CI: $1,626-$4,692). When other direct medical costs were included raltitrexed became cost saving. CONCLUSIONS: Raltitrexed offers a more convenient treatment regimen than 5-FU plus leucorvorin and is as effective while causing less toxicity.

PP60. A HEALTH ECONOMICS ASSESSMENT OF THE CONSEQUENCES OF INCREASED INTAKE OF FRUITS AND VEGETABLES

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Based on a 20% population sample of 5 years data from the National Bureau of Statistics this assessment will quantify the health economics consequences on the Danes if they were to increase their intake of fruit and vegetables from the present 280 g per day to 600 g per day, and if the health advantages discribed in the literature came through with full force right away.

A model is developed based on the statistical data, which describes the health consequences in terms of fewer days lost through sickness and more saved life years, and the related savings in the health expenditures will be calculated. The savings in resource use in the health sector will be converted in monetary units by using national DRG-prices and other available cost figures, while the possible gain in productivity as a result of fewer days lost through sickness and gained lifetime will be seen in relation to the gross national product.

The aim of this assessment is primary to inform decision makers about the scale of benefits that possibly can be achieved if the epidemiological evidence of reduced morbidity and mortality holds, and the population can be influenced to increase their intake of fruits and vegetables to the recommended levels. The analyses and the models that the analyses are based on, can, however, be used in other connections, first and foremost for analysis of the various interventions relative/comparative cost-effectiveness of different interventions targeted at certain groups. It could also be used to assess for which population groups it would be the most relevant to aim a campaign towards, in order to get the highest possible effect per resource unit. These effects could be expressed in the form of expected savings in days lost through sickness and gained life years, or QALY's.

Furthermore, the calculations could be used in cohorte analyses to describe future consequences of the intervention for a generation of the population or for a specific risk group (e.g. 20-year-olds or people from low socio-economic groups).

PP61. THE INFLUENCE OF PHARMACOECONOMIC INFORMATION ON DECISION-MAKING IN HOSPITALS

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INTRODUCTION: Over the last 15 years pharmacoeconomics research has grown rapidly, but little is known about the dissemination and the actual use of economic information in decision-making. We conducted a literature review of papers addressing the use of economic information in drug selection for hospital formularies to determine its role in decision-making, the barriers that prevent its use and the importance of these barriers.
METHODS: Five bibliographic databases were searched: (1) Medline, (2) Embase, (3) Pascal, (4) NHS Economic Evaluation Database, and (5) International Pharmaceutical Abstracts, from 1991 to 1998. In addition a manual search of the journal PharmacoEconomics and of the reference sections of all retrieved papers was performed. To appraise and summarise the publications we used a 7-point checklist.
RESULTS: We assessed 34 papers. Case studies based on personal observations were reported in 27 (79%) papers, surveys in 5 (15%) and literature reviews in 2 (6%). Input that were reported to have a greater impact on decisions than economic information were: (1) the efficacy and safety of drugs (mentioned in 100% of the papers), (2) dosage and administration procedures (50%), (3) quality of life considerations (32%), and (4) clinical experience of practitioners (29%). The most important of the seven identified barriers to the use of economic information in decision-making were: (1) lack of credibility of economic evaluations (65%), (2) economic data did not apply to the setting of the decision-makers (62%), (3) decision-makers had no expertise in appraising economic information (59%), (4) decision-makers did not have economic information and it was not possible to collect it (47%), and (5) lack of collaboration between producers of economic information and decision-makers (41%).
CONCLUSIONS: The current use of economic information in decision-making is limited compared with its potential use. More research is needed to determine decision-makers' needs for economic information and to identify incentives to take it into account. We will perform a survey of French hospital pharmacists to investigate these issues.

PP62. SURVIVAL IN PATIENTS WITH METASTATIC BREAST CANCER: META-ANALYSIS OF RANDOMISED STUDIES COMPARING ORAL AROMATASE INHIBITORS WITH MEGESTROL

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In patients with metastatic breast cancer, oral aromatase inhibitors can improve survival in comparison with megestrol. We conducted a meta-analysis to assess the effectiveness of oral aromatase inhibitors (letrozole or anastrozole or exemestane) as compared with megestrol. Our study included all randomised controlled trials published in English from January 1970 to 15 March 2000. After a MEDLINE search, 3 trials were found to meet our inclusion criteria. A total of 1648 patients, that were enrolled in these trials, were included in the survival meta-analysis. Our methodology retrieved patient-level information from all of these subjects; survival up to 40 months after randomisation was compared between the two treatment options.
The results of our meta-analysis showed that, in comparison with megestrol, oral aromatase inhibitors prolonged survival at levels of statistical significance (relative death risk for oral aromatase inhibitors was 0.80, 95%CI of 0.69 to 0.91; p=0.015 by Cox analysis). The inter-trial heterogeneity was statistically significant. A lifetime analysis of the pooled survival curves for aromatase inhibitors vs. megestrol found a mean survival gain of 3.7 months per patient. The survival gain per patient, determined separately for individual drugs in comparison with megestrol, was 4.0 months for letrozole, 2.8 months for anastrozole, and 4.4 months for exemestane. The survival curve for letrozole, however, did not differ statistically from that of megestrol.
Our results showed that oral aromatase inhibitors improve survival in this disease condition, but potentially important differences were found between individual agents.

PP63. IRINOTECAN COMBINED WITH FLUOROURACIL VS. FLUOROURACIL ALONE IN METASTATIC COLORECTAL CANCER: COST-EFFECTIVENESS ANALYSIS

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Background: Oncologic treatments that improve survival are often subjected to a pharmacoeconomic evaluation that determines the cost per life year gained (ratio of incremental cost and incremental effectiveness, where both values are estimated on the long term or with a lifetime perspective). The recent study by Douillard et al. (Lancet 2000;355:1041-1047) has shown that, in patients with advanced colorectal cancer, the combination of irinotecan and fluorouracil, given as first-line treatment, significantly improves survival in comparison with fluorouracil alone.
Patients and methods: We analysed the survival data published in Figure 3 of Douillard 's study to estimate the lifetime survival gain per patient (or incremental effectiveness) resulting from this innovative combination treatment. For this purpose, we used a standard Gompertz analysis with survival extrapolation after 27 months. The cost of irinotecan was obtained from current prices in Italy (1.7 Euros per mg) and in the UK (£ 1.3 per mg). The incremental cost per patient was estimated on the basis of an average cumulative dose of irinotecan of 4,820 mg per patient.
Results: Our analysis showed that the survival gain was 2.0 months per patient (mean survival = 17.8 and 15.8 months per patient in the irinotecan group and in the control group, respectively)
In the economic comparison between these two treatments, the irinotecan group had an incremental cost of £6,267 per patient or 8,215 Euros per patient. These data show that the use of irinotecan as adjunctive therapy in this disease condition has a cost per life year gained of £37,602 (or 49,290 Euros). These figures remained virtually unchanged after introducing 3% annual discount for both costs and survival.
Conclusions: On the basis of our results, the cost-effectiveness ratio of irinotecan in advanced colorectal cancer is around 50,000 Euros per life year gained, which is generally considered an unfavourable value

PP64. DEVELOPMENT OF A SYSTEMIC THERAPY COSTING MODEL IN A PROVINCIAL ONCOLOGY PROGRAM

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BACKGROUND: Our agency sets standards, and is financially responsible for care of all cancer patients in the province. Socialized medicine in our country does not permit practice of 'two-tiered' medicine. Thus, sufficient funding must be secured to treat all eligible patients before a new treatment is used. A costing model to compare systemic cancer therapy treatment protocols is required to determine incremental changes in budget and resources.
METHODS: Detailed time and motion study comparing 2 metastatic breast cancer protocols, (paclitaxel (P), docetaxel (D), each given every 3 weeks for up to 6 cycles), was conducted and recorded into a complex model using Excel®. A simple model was designed concurrently, and the same 2 protocols were evaluated. Subsequently, these 2 methods were combined to create an efficient, detailed costing model.
RESULTS: The complex model P and D per cycle costs were: labour $93 and $75; equipment $1.50 and $1.50; supplies $30.50 and $9; drugs $1290 and $1940; total $1415 and $2028 respectively. This was further broken out into costs for administration, dispensing, and full-time equivalent employees. The simple model total per cycle costs were: $1375 and $2007 respectively. The combined model costs were: $1427 and $2053 broken down into dispensing, administration, labour, supply, and drug costs. Time on the chemotherapy unit was built into this model: 210 versus 90 minutes per cycle respectively. All 3 models provided similar overall cost estimates, however, the combined model most efficiently provided the most detail.
DISCUSSION: The model permits cost-minimization analyses. Technology is currently being developed that will link costing data to survival and outcomes data, making cost-effectiveness analyses possible.
CONCLUSIONS: The cost of treatment protocols are being determined and compared to facilitate budget considerations, government funding applications, and efficient use of resources. An adaptable systemic therapy oncology costing model has been developed and tested.

PP65. COSTS AND REIMBURSEMENT OF DIAGNOSIS, TREATMENT AND FOLLOW-UP OF PATIENTS WITH ACUTE MYELOID LEUKAEMIA IN THE NETHERLANDS

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OBJECTIVE: To calculate the costs in various treatment phases of acute myeloid leukaemia (AML) and to compare it with the hospital reimbursement.
PATIENTS AND METHODS: Patients less than 65 years, who were treated at two university hospitals for newly diagnosed AML in the period 1994-1995 were included. The cost analysis distinguished between diagnosis, treatment, follow-up (maximum of 2 years) and treatment of relapse. The treatment period was divided into remission induction and consolidation treatment, harvest of bone marrow or stem cells and transplantations. Patients could receive autologous bone marrow transplantation (auto BMT), autologous stem cell transplantation (auto SCT), allogeneic BMT or allogeneic SCT. Only direct medical costs based on real cost prices have been taken into account. Furthermore, the hospital's reimbursement has been calculated.
RESULTS: The costs of diagnosis amounted to US$ 3167. Remission-induction treatments cost on average US$ 46387 and harvest of bone marrow or stem cells cost US$ 6491. The costs of the applied transplantations varied between US$ 25531 and US$ 44087. The average costs of transplantation were US$ 19838. Costs of follow-up amounted to US$ 4167. Relapse treatment mainly consisted of re-induction therapy. Treatment of relapse cost on average US$ 24338. The total average costs of AML patients amounted to US$ 104386, as the reimbursement of the hospital was US$ 34500.
DISCUSSION: Treating AML patients is very expensive and additional reimbursement is required. It does not seem likely that major reductions in costs will appear in the next future. When efficacy and effectiveness are taken into account, it seemed that choices based on costs could be made between several consolidation techniques and between a specific consolidation technique and/or palliative treatment. However, as this study is based on 'ongoing' clinical trials, the results of these trials should be awaited to make a definite conclusion.

PP66. QUALITY OF LIFE IN PATIENTS WITH NON-SMALL CELL LUNG CANCER

Vaiani M. and the "Quality-of-life Study Group" *of Società Italiana di Farmacia Ospedaliera and Istituto di Economia Sanitaria, c/o Laboratorio SIFO di Farmacoeconomia, Drug Information Center, Florence, Italy.*

Introduction. There is a growing interest in measuring patients' quality of life (QOL) both in controlled clinical trials and in longitudinal or cross-sectional epidemiologic studies. These measurements are aimed at estimating how QOL is influenced by a specific disease condition or by a given therapeutic intervention. The objective of our study was three-fold: 1. To measure QOL and utility in a series of patients with non-small cell lung cancer using two standard generic questionnaires (SF-36 and EuroQol); 2 To evaluate the impact of some clinical variables on QOL; 3. To assess the correlation between the QOL measurements produced by the two questionnaires.
Patients and methods. Our study included 15 Italian hospitals. A total of 95 patients with non-small cell lung (93% male, mean age = 62 years) were asked to complete the SF-36 and the EuroQol questionnaires. For each patient, the following clinical information was recorded: presence of metastasis; tumour resection; administration of chemotherapy and/or radiotherapy; awareness of diagnosis.
Results. The mean scores on the 8 domains of the SF-36 ranged from 20.8 (physical role) to 63.0 (social functioning). The physical and mental summary scores of the SF-36 had an average of 36.1 (range: 13.2 to 59.1, SD 9.7) and 40.2 (range: 11.5 to 66.0, SD 13.2), respectively. The $EuroQol_{self\ classifier}$ showed a mean score of 0.58 (range: −0.59 to 1.00, SD 0.32), while the Euro Qol_{VAS} produced a mean score of 0.58 (range: 0.07 to 1.00, SD 0.20). Among the clinical variables included in our analysis, only the presence of metastasis was shown to significantly affect QOL. Both the Euro $Qol_{self\ classifier}$ and the $EuroQol_{VAS}$ showed statistically significant correlations with all the SF-36 scales.
Conclusions. Our study has quantified the degree to which QOL and utility are impaired in patients with non-small cell lung cancer.

PP67. DIFFERENCES IN QUALITY OF LIFE BETWEEN PATIENTS UNDERGOING STEREOTACTIC LARGE-CORE NEEDLE BIOPSY OR OPEN BREAST BIOPSY FOR THE DIAGNOSIS OF NONPALPABLE BREAST DISEASE.

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Introduction: Image guided large-core needle biopsies are increasingly replacing needle localised open breast biopsies for the diagnosis of nonpalpable breast disease. At the end of 1997, a multicenter study was initiated in the Netherlands, addressing diagnostic accuracy and cost-effectiveness of stereotactic large-core needle biopsy (COBRA study (COre Biopsy after RAdiological localisation). In the context of this study, we compared quality of life during the diagnostic interval among patients undergoing either large-core needle biopsy or open breast biopsy.
Patients and Methods: 27 consecutive patients with nonpalpable breast disease underwent open breast biopsy in four different hospitals in the Netherlands (open biopsy group). This group was compared with 30 consecutive patients undergoing large-core needle biopsy of nonpalpable breast lesions in four different hospitals (needle biopsy group). Quality of life was assessed using standard questionnaires (EQ5D, SF 36). These questionnaires were applied one day before and four days after the diagnostic intervention.
Results: One day before the diagnostic intervention, utility measured with EQ5D was slightly lower in the open biopsy group than in the needle biopsy group (69 versus 73 resp., p=0.05). Four days after the diagnostic procedure, utility scores were significantly lower in the open biopsy group (61 versus 71 in the needle biopsy group, p<0.001). Analysis of the results obtained by means of the SF 36 questionnaire demonstrated that the open biopsy group scored significantly lower for physical functioning, physical performance and social functioning and experienced more pain after the diagnostic intervention.
Conclusion: During the diagnostic interval, patients undergoing stereotactic large-core needle biopsy experience better quality of life than patients undergoing needle localised breast biopsy for the diagnosis of nonpalpable breast disease. A policy decision, however, should not be made without taking into account diagnostic accuracy.

PP68. SIMULATION MODELING FOR THE MANAGEMENT OF A REGIONAL MEDICAL ONCOLOGY SYSTEM

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This presentation demonstrates the construction and use of simulation models for exploring the effect of changes in therapy and follow-up regimens upon the performance of a regional cancer system. Outputs of the model are response paths for patient survival, for medical oncologist workload, and for cancer system costs arising from changes in therapy or follow-up regimens. These responses, in turn, can affect patient or clinician decisions to choose particular treatments, and can change over time the flows of patients under care. Cancer system managers are also interested in the effect upon their systems of population growth and aging, and in the effects of changing disease incidence and earlier disease staging which might arise from prevention or screening initiatives taken earlier. This simulation model is specific to colon cancer in the Ontario cancer system, but the methodology and the model are broadly applicable to other cancer sites elsewhere.

Although industry and engineering have long used simulation techniques to assist in managing their systems, the health care system has to date made little managerial use of this tool. Recent developments in simulation software make the models easier to construct and operate and provide powerful display features which can be useful in gaining clinical and management understanding of economic questions.

The model is constructed with **ithink** © v6.0 software, (High Performance Systems Inc., Dartmouth, NH, USA) a tool with considerable potential appeal for health economists because of its ease of use, analytical power and display capabilities. A principal purpose of this presentation is to introduce the software to cancer economists and managers who may not have encountered it.

PP69. COST IDENTIFICATION OF CONCOMITANT AND ADJUVANT TEMOZOLOMIDE TO RADIATION TREATMENT FOR NEWLY DIAGNOSED GLIOBLASTOMA.

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Background
Temozolomide (TMZ), an oral alkylating agent, has been recently approved for recurrent glioblastoma. A pilot phase II trial was initiated with TMZ as a first line therapy along with radiotherapy. As new therapeutic modalities are increasingly expensive, we assessed the marginal direct cost of this treatment.
Patients and methods
After surgery or biopsy, patients received standard radiotherapy with concomitant TMZ (75 mg/m2/d) 1 hour prior radiation for 6 weeks, followed by adjuvant TMZ (200 mg/m2/d x 5) for 6 cycles. Follow-up consisted of medical visits, blood tests, and MRI every other month in order to detect relapse.
Cost assessment singled out the concomitant TMZ, the adjuvant TMZ, and follow-up phases. Personnel costs were computed as wages x time, and drug, imaging and laboratory tests as prices. Protocol-driven costs were excluded, and toxicity will be computed separately.
Results
Forty-two patients (26 men, 16 women, mean age 52 yrs, range 24 to 70) were included. Adjuvant therapy is still ongoing in 10 pts, and planned in 5 pts. Eleven pts did not receive adjuvant therapy because of tumor progression, toxicity or pt refusal, and 8 pts dropped from adjuvant TMZ because of tumor progression. Theoretical drug acquisition cost for complete concomitant TMZ would amount to CHF 12'026±1'331 and CHF 19'062±3'692 for complete adjuvant TMZ.
Observed distribution of costs is displayed below:

	Concomitant TMZ (CHF, n=42)	Adjuvant TMZ (CHF, n=26)	Follow-up (CHF, n=28)
Visits	154±73	195±89	91±88
TMZ	10'567±2'895	13'727±6'612	0
Imaging	0	134±320	466±603
Laboratory tests	255±157	276±148	114±181
Total	**10'975±2'900**	**14'332±6'818**	**671±676**

Conclusion
Temozolomide may be an effective drug as an adjuvant therapy after radiotherapy in pts with glioblastoma. It can be administered orally as an outpatient. Most of the costs were related to drug acquisition. Definite cost-effectiveness/utility assessment should be included in a phase III randomized trial.

PP70. SHOULD HIGH-RISK POPULATIONS BE ROUTINELY TESTED FOR BRCA1/2 MUTATIONS? A COST-EFFECTIVENESS ANALYSIS

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Breast cancer is a disease in which early detection significantly increases survival, and where prophylactic strategies can decrease the risk of developing breast cancer by up to 90%. Individuals at high risk face a lifetime probability of developing breast cancer eight times greater than that of low-risk individuals. Furthermore, the costs of treating early stages of breast cancer are considerably less than the costs of treating advanced stages. However, prophylaxis is often postponed until an individual acquires information that necessitates preventive action. This not only affects the individual's probability of survival, but also drains health care funds to treat advanced breast cancers, which could otherwise have been used elsewhere.

This paper analyses whether high-risk populations (such as Ashkenazi Jewish women) should routinely be tested for BRCA1/2 mutations. The analysis incorporates the probabilities of developing breast cancer, the costs of treatment and the quality of life in various health states to assess whether it is indeed cost-effective to screen certain populations. This is presented as a decision analysis (using DATA™ software) which follows standard expected utility theory and in which decisions are made under uncertainty.

PP71. HOSPITAL SERVICE USE ASSOCIATED WITH CHEMOTHERAPY-INDUCED EMESIS AND NAUSEA FOR PATIENTS WITH PRINCIPAL OR SECONDARY DIAGNOSES OF CANCER.

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Objective – Health service utilization may be increased for cancer patients with chemotherapy-induced emesis or nausea (CIEN). However, there is no well-established evidence of this relationship in the literature. We examined hospital length of stay for patients with CIEN, compared to patients without CIEN.

Method – Data used for this study were the 1996 Healthcare Cost and Utilization Project (HCUP) from the Agency for Health Care Policy and Research in the U.S. The data contained detailed information for over 5 million hospital admissions from 900 hospitals. All admissions with cancer as the principal or secondary diagnoses and with chemotherapy as the principal procedure were included in this study. ICD-9 codes were used to define cancer, emesis, nausea, as well as chemotherapy procedure. Multivariate analyses, controlling for age, gender, race, and comorbid conditions, were performed to compare the length of stay between patients with CIEN and patients without CIEN. Sub-analyses were performed by cancer type. Expanded analyses were performed to include radiation therapy as the principal procedure in addition to chemotherapy.

Results – A total of 64,330 hospital admissions meeting the inclusion criteria were identified from the database; 4,472 of them were reported to have had CIEN. The length of stay for patients with CIEN was 1.7 days longer than that for patients without CIEN ($p<0.001$). Sub-analyses and expanded analyses demonstrated similar results.

Conclusion – Reported CIEN was associated with a longer hospital stay for patients with principal or secondary diagnoses of cancer. Therefore, effective preventive therapy for CIEN may reduce health care utilization.