PP61. Adaptation of pharmacoeconomic software

Malfair Taylor SC
British Columbia Cancer Agency, Vancouver, BC, Canada

Background: A pharmacoeconomics service was recently developed at this provincial oncology centre. The new service was faced with the challenge of proving its usefulness with limited resources and equipment. Without any initial budget for pharmacoeconomics software, it was decided that a free-of-charge demonstration program would be adapted and used.
Methods: Pharmacoeconomic cost analysis software (PECAN Version 2.5.) was provided courtesy of Glaxo Wellcome. This software was designed specifically to provide a cost analysis for metastatic breast cancer. The manipulation of this software was undertaken to facilitate analyses of other sorts of cancer. Metastatic colorectal cancer was chosen as the next disease model. As part of a prospective pharmacoeconomic analysis, data collection forms were developed and utilized to capture costs including clinic visit, laboratory, physician time, nursing time and materials, pharmacy time and materials, drug acquisition, and patient out-of-pocket expenditures. Literature evaluation was used to determine adverse effect rates, and costs of managing these were incorporated. Collected data was averaged and entered into the software program. Upper and lower limits of ranges of collected data were used for sensitivity analysis.
Results: The PECAN software was successfully adapted to facilitate the cost analysis of two metastatic colorectal cancer treatment regimens.
Discussion: The successful adaptation of the PECAN software to the metastatic colorectal cancer model has allowed the pharmacoeconomics service the opportunity to demonstrate its capabilities. The service may be accessed to aid in decisions regarding guidelines, policies, and formulary requests. It is also available to investigators wishing to perform a pharmacoeconomics analysis or add a pharmacoeconomic component onto a clinical trial. As the service becomes more widely accessed, it is proposed that supportive funding will increase and newer software requiring fewer manipulations may be purchased. This undertaking has shown how a pharmacoeconomic analysis can be performed without monetary investment into a pharmacoeconomics software program.

Malfair Taylor SC, BC Cancer Agency, Pharmacy Department, 600 West 10th Ave., Vancouver, BC, V5Z 4A6, Canada

PP62. Cost/effectiveness assessment of cytogenetic and molecular biology analysis for acute leukemia's prognosis

Tonnaire G[1], Gabert J[2], Lafage M[2], Sainty D[2], Maraninchi D[2], Moatti JP[1]
[1]INSERM U379, Epidemiology and Social Sciences Applied to Medical Innovation, Institut Paoli-Calmettes, Marseille, France; [2]Institut Paoli-Calmettes, Marseille, France

Background: Some chromosomal abnormalities clearly appear as prognostic factors in acute leukemia. Using a cost/effectiveness analysis, we tried to determine the best strategy for diagnosing these abnormalities. Cytogenetic and molecular analysis were chosen for assessment. There are already numerous clinical and technical articles comparing these techniques, but they have never been assessed in terms of cost/effectiveness ratios. The aim is to show how these two techniques can substitute, or complement, one another. There is also the question of assessing the value of supplementary information obtained by cytogenetic analysis.
Method: Eleven possible strategies have been identified and analysed. 107 adult patients with de novo myeloid or lymphoid acute leukemia at diagnosis, were tested in 1995, in a single institution, by the two techniques. The anomalies retained are, on one hand, those identifiable by both techniques, i.e. the translocations t(9;22), t(8;21), t(15;17), t(4;11), t(1;19), the inv(16), and, on the other hand, some anomalies that can only be detected by cytogenetics such as monosomy 5 or 7 (or deletion of their long arms) and trisomy 8. All those anomalies constitute a group of well known prognostic markers. The effectiveness criterion is the rate of detection for the anomaly for each strategy.
Results: Considering the anomalies identifiable by both techniques, we got a rate of 18.5% with each procedure, whereas adding anomalies only detectable in cytogenetic, the rate for the cytogenetic analysis goes up to 30.8%. The cost of molecular biology obtained is US$ 241.20 for an analysis with a single parameter studied (i.e. one anomaly) and US$ 94.80 per supplementary parameter studied. The average cost of cytogenetic analysis is US$ 577.40. Whatever the number of parameters studied by molecular biology (1 to 4), cytogenetic analysis is more expensive.
Discussion: The cost/effectiveness ratios show the following results: 1 - the most cost/effective strategies are those using only one technique (cytogenetic or molecular biology); 2 - for the anomalies identifiable by both techniques and effectiveness being identical for the two types of analysis, the molecular biology is more cost/effective; 3 - if one considers all the anomalies, the molecular biology has a lesser diagnostic effectiveness than the cytogenetic; 4 - strategies combining the techniques successively (PCR and cytogenetic for failure and negative results) are more cost effective than strategies which combine simultaneously the techniques, without any loss of effectiveness. From these results from a single institution, multicentric studies of cost/effectiveness comparing a recent technology entering the hospital field (the PCR technique) and the standard technique (classical cytogenetic) are warranted in order to assess their impact in terms of health care.

Tonnaire G, INSERM U379, Institut Paoli-Calmettes, 232 Bld Sainte Marguerite, 13273 Marseille Cedex 9, France

PP63. Statistical inference and sample sizes for cost-effectiveness analyses

van den Hout W
Leiden University Medical Center, The Netherlands

Background: The aim of the presentation is to show unfavourable statistical properties of the cost-effectiveness ratio when the difference in costs or effects is not clear-cut and to propose more adequate alternatives.
Results: Consider a clinical trial that provides estimates of the differential cost ΔC and health effect ΔE of a certain policy decision, for example introducing a new medical intervention. A possible decision criterion is whether the CE-ratio $R=\Delta C/\Delta E$ is acceptable: $\{R \leq R^*\}$. The acceptability threshold R^* could for example be chosen equal to $R^*=50.000\$/QALY$. A disadvantage of this ratio criterion is that it is unstable when the effect ΔE is unclear and that negative ratios can be both favourable ($\Delta C \leq 0 < \Delta E$) and unfavourable ($\Delta E < 0 \leq \Delta C$). A better criterion is whether the cost are small compared to the effect: $\{\Delta C \leq R^* x \Delta E\}$. A disadvantage of this criterion is that it can be non-monotone. Consider two different acceptability thresholds $R^* < R^{**}$. Even if the estimated cost ΔC and effect ΔE are positive, the seemingly stricter criterion can be more probable: $Pr\{\Delta C \leq R^* x \Delta E\} > Pr\{\Delta C \leq R^{**} x \Delta E\}$. This counterintuitive behaviour can be prevented if probabilistic statements about cost-effectiveness are not separated from statements about costs or effects, that is if the probability is calculated for combined statements like $\{R \leq R^*$ and $\Delta E \geq 0\}$ or $\{R \leq R^*$ provided $\Delta E \geq 0\}$. The probability of these criteria are monotone in R^*. An approximate procedure is provided to determine the required sample size for these criteria.
Discussion: CE-ratios from trials in which either costs or effects are not clear-cut should be treated with suspicion unless this uncertainty is explicitly taken into account.

van den Hout W, Leiden University Medical Center, Medical Decision Making Unit, D6-27, PO Box 9600, 230 RC Leiden, The Netherlands

PP64. Resource utilisation in intensive chemotherapy, autologous versus allogeneic bone marrow transplantation in acute myeloid leukemia

Zittoun RA, Mandelli F, Suciu S, Keating S, Dardenne M, Berneman Z, De Witte T, Willemze R, Van Der Heyden M for the EORTC and GIMEMA Leukaemia Cooperative Group

Background: Following an induction chemotherapy, patients achieving a complete remission receive a first intensive consolidation course. Then, this is followed by allogeneic bone marrow transplantation if an HLA identical

donor can be located (allo-BMT), while others are randomised to a second consolidation chemotherapy or autologous bone marrow transplantation (ABMT). If there is no clear survival benefit for either of these, other end points like disease free survival, treatment related morbidity and the costs of treatment will be given more importance.
Methods: This is a retrospective analysis based on the EORTC AML 8 study, opened in june '93 and closed in june '94, comparing the three treatments mentioned. The case report forms of the clinical trial contained the following variables of relevance for an assessment of resource utilisation: number of days hospitalised, number of days in protected environment, supportive care given (eg transfusions, use of antibiotics), number of infectious episodes, number of days with fever. The cost calculations will be based on the resource utilisation data from the trial and unit prices (charges) from the Belgian health insurance and reimbursement system.
Results: 941 patients entered the AML 8 study. 576 entered and remained into complete remission after induction and first intensive consolidation. Out of these, 137 with an HLA identical sibling were allografted, the other patients were randomised between ABMT (N = 117) and second intensive chemotherapy (N = 112). There were no differences between the alternatives with respect to overall survival, while for disease free survival and relapse risk allo-BMT was most favorable, followed by ABMT and chemotherapy in that order. Treatment related morbidity was smallest for chemotherapy. This preliminary analysis contains only a comparison of resource utilisation. For all types of resource utilisation, the consumption was smallest for second intensive consolidation. Regarding the two types of BMT, none is uniformly most demanding: number of hospital days for allo-BMT patients is about 9% higher as the number for ABMT, while the number of transfusions is 40% higher for ABMT.
Discussion: No valuation of outcomes has been attempted in this analysis, which is only concerned with some -important - elements of direct costs. As in all retrospective analyses, some important variables have not been included because of lack of data. Notably, for allo-BMT the costs of locating an HLA identical sibling has not been included as main endpoint in the AML 8 trial. Another issue that has not been included is the prevention or/and treatment of graft versus host disease (GVHD); this will be an important item in the planned cost evaluation, since we know that despite prevention for almost all patients eligible for allo-BMT, ± 60% of the allografted patients had GVHD and half of these were actually treated for this.

Van Der Heyden M, EORTC Health Economics Unit, Avenue E. Mounier 83/Bte 11, 1200 Brussels, Belgium

PP65. Economic evaluation of high dose chemotherapy for breast cancer patients

van Enckevort PJ[1], TenVergert EM[1], de Vries EGE[2], Rodenhuis S[3]
[1]Office for Medical Technology Assessment; [2]Departement of Medical Oncology, University Hospital Groningen, Groningen, The Netherlands; [3]The Netherlands Cancer Institute, Amsterdam, The Netherlands

Introduction: Hard evidence on the effectiveness and cost-effectiveness of high dose chemotherapy (HDC) in combination with peripheral blood progenitor cell transplantation (PBPCT) as adjuvant treatment for breast cancer patients is still lacking. To date, no randomised clinical trials have been reported in which the effectiveness of HDC-PBPCT was evaluated. Moreover, cost-effectiveness data are scarce, not only for HDC-PBPCT, but also for the adjuvant treatment of breast cancer patients in general. Most of these economic evaluations have methodological drawbacks. For instance, no economic evaluation integrated in a clinical trial was performed, only direct medical costs were included, and mostly costs were based on charges. At this moment, a single Dutch national randomised study with an integrated economic evaluation is in progress, in which HDC-PBPCT is evaluated. In June 1997, 525 patients were randomised. First results of the study are expected in the year 2000.
Study design: In the Dutch randomised study, patients with four or more positive lymph nodes are included. Standard dose chemotherapy consisting of five cycles 5-fluorouracil, epirubicin, and cyclophosphamide is compared with four identical cycles and one cycle with HDC (cyclophosphamide, thiotepa, carboplatin) followed by PBPCT. Apart from clinical endpoints, a quality of life analysis and an economic evaluation are performed. For this study consensus was reached between all university hospitals and the two cancer centres in the Netherlands.
In the economic evaluation, firstly, a cost-effectiveness analysis with disease-free survival as effect parameter will be performed. This analysis will be based on the observed costs and disease-free survival of the patients during the study period. Secondly, a cost-effectiveness analysis with overall survival as effect parameter, and, thirdly, a cost-utility analysis with quality adjusted survival (Qaly's) as effect parameter, will be executed. Those two analyses will be performed from a lifetime perspective. Long-term survival will be estimated on the basis of the observed disease-free and overall survival, lifetime costs on the basis of those survival figures and the observed costs of the patients during the different stages (e.g. treatment, period with relapse, period without relapse, final stage). Costs are assessed from a societal perspective, and, where possible, full resource costs are estimated. The following types of costs are included in the analyses: direct medical costs, direct non-medical costs and indirect non-medical costs.
Presentation: In the presentation, firstly, a brief literature review of economic evaluations of the adjuvant treatment of breast cancer patients between 1980-1996 will be given. Secondly, the major drawbacks of those economic evaluations will be addressed. Thirdly, the study design of the Dutch study on HDC-PBPCT will be presented, and it will be addressed how some of the drawbacks in the reviewed economic evaluations have been solved in this study.

van Enckevort PJ, University Hospital Groningen, Office for MTA, P.O. Box 30.001, 9700 RB Groningen, The Netherlands

PP66. Using appropriate comparators in economic evaluations: An exercise for Belgium

Van Tigggelen O[1], Storme G[2], Torfs K[3], Van den Berge D[2], De Coene N[2]
[1]CGZ, Centre for Health Economics and Hospital Management, VUB, Brussels, Belgium, [2]Department of Radiotherapy, Oncology Centre, AZ - VUB, Brussels, Belgium, [3]Health Economics Unit, European Organisation for Research and Treatment of Cancer (EORTC), Data Centre, Brussels, Belgium

Background: Standard effective treatments, but less challenging and rewarding might be overlooked in clinical and economic research, while new but often more expensive treatments with only modest or no improved effectiveness in comparison to them, receive relatively more attention. This may lead to inefficient allocation of health care budgets.
Purpose: The consequences of including standard effective treatments in the evaluation of different treatments for early breast cancer in premenopausal women (T0-3,N0-2,M0) and in non-Hodgkin lymphoma, both diseases with a markedly increasing incidence and associated with potentially high costs.
Material and methods: The effectiveness of alternative treatment strategies is assessed on the basis of a review of important medical literature. An exercise in the context of the Belgian health care insurance system compares the expected charges to be paid for different treatment strategies.
Results: Ovariectomy in Breast Cancer (770 ECU) and conventional chemotherapy "CHOP" (2,740 ECU) in non-Hodgkin lymphoma have proven their effectiveness. According to charges fixed by the Belgian health care insurance system, substantial savings in comparison to respectively treatment with chemotherapy 1,900 ECU in a day care and 2,870 ECU in hospitalisation). Costs of the treatment in non-Hodgkin lymphoma with chemotherapy LNH84 versus CHOP versus autologous bone marrow transplantation are estimated at 2,750 ECU, 7,200 ECU and 19,220 ECU, respectively.
Discussion: Health care authorities should order and fund appropriate research in cancer care to independent observers in order to maximise their population's total health within a given limited budget. In cost-effectiveness studies regarding cancer care all relevant available treatment options should be incorporated.

Van Tigggelen O, AZ-VUB, CGZ, Laarbeeklaan 101, 1090 Jette-Brussels, Belgium