PET is an expensive technology, and its benefits in terms of detection and lives saved, over other imaging modalities must be compared against its additional costs.
Methods: We conducted a decision analysis in four areas of oncology: breast, cervical, lung and colonic. The care pathways and subsequent projected outcomes in each were evaluated for PET versus alternative diagnostic strategies. The costs and benefits were evaluated at each of four stages: presence of abnormality; determination of malignant or benign tumour, accurately staging the disease and early detection of recurrence. In each case based upon the best and worst sensitivities and specificities for PET and its alternatives.
Results: Considering results with regard to the number of cases detected per 1000 patients presenting with symptoms for each of the four cancer groups, PET was the dominant technology in the diagnosis (and subsequent treatment management) of lung cancer and breast cancer. In the diagnosis of colon and cervical cancer PET did not dominate over the alternative technologies (e.g. CT, MRI, biopsy, endoscopy, ultrasonography in combinations). For lung cancer, PET led to an increase of between 80 and 612 life years over the next best technology. The cost per life year saved of using PET was between £1,079 and £2,659 versus that of the next best alternative, in each case, of between £1,810 and £3,081. This translates into a cost advantage, for PET, of between £101 and £422 per life year saved. For breast cancer, PET led to an increase of between 278 and 1388 life years over the next best technology combination. The cost per life year saved of using PET was between £1,430 and £1,453 versus that of the next best alternative, which was between £1,019 and £1,502. This translates into a cost difference for PET, of between £72 less per life year saved over the next best alternative, to £434 more per life year saved.
Discussion: PET will not be the technology of choice at all four stages of the diagnostic process for each of the four cancers. While PET will frequently be a more accurate diagnostic technique compared to its alternatives, the marginal gain in accuracy will not be sufficient to justify the large increase in costs. The project identified the stages in each of the four oncological areas where PET contributed most in terms of cost effectiveness and should be the technology of first choice in the detection of cancer.

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OP15. Use of the EuroQoL among patients receiving radiochemotherapy for pancreatic cancer: Psychometrical tests and quality adjusted survival analysis

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Background: Cost-utility analysis of medical technologies applied to seriously ill patients requires health-related quality of life (QoL) measures that a) do not overstress the patient and b) provide reliable, valid and sensitive data from which utility weights for the calculation of QALYs can be obtained. The EuroQoL is a generic index measure that is easy to understand and can be self-completed by the respondent within less than 10 minutes. The reliability and validity of the EuroQoL has been shown in the general population as well as in patient groups with selected diseases. However, the EuroQoL has hardly been tested among seriously ill patients. In this study, the EuroQoL is applied to patients with inoperable pancreatic cancer who participate in a clinical phase II study of radiochemotherapy. The study was started in January 1997 and is still in progress. The purpose of our study is 1) to evaluate the practicability and psychometric characteristics of the EuroQoL among these patients, 2) to compare health-related utility weights of this patient group with those from the general population, 3) to assess the effect of subjective expectations with respect to treatment success and 4) to perform quality-adjusted survival analysis. Cost-measurement and cost-utility analysis are intended in another part of our study.
Methods: All inoperable pancreatic patients who present at the Ulm university hospital and meet the inclusion criteria of the clinical study are consecutively enrolled in this study. QoL assessment is conducted during the entire course of therapy. Patients are interviewed during intra-arterial chemotherapy and complete the EuroQoL questionnaire during each of theirs stays at home between two treatment episodes. Practicability is assessed by rejection rates and patient comments. Test-retest reliability is evaluated by the ICC. Construct validity is shown by correlating QoL data with clinical parameters. Responsiveness of VAS values is judged by Guyatt's responsiveness statistic and ROC curves which are calculated on the basis of the results of a transition question. For each patient QALYs are computed by quality adjusted survival analysis.
Results (study still in progress): Preliminary results indicate that the EuroQoL is well accepted by this group of patients. However, results of a pilot study showed, that the original reliability test over-stressed the patients, and hence had to be abbreviated. The EuroQoL seems to be very responsive and able to well discriminate between stays in hospital and at home. Patients in our study tend to rate their health states on the VAS scale much higher than the general population rates these states.
Discussion: Preliminary results indicate good practicability and responsiveness of the EuroQoL in this group of seriously ill patients.

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OP16. Cost-effectiveness and quality of life evaluation, in the context of current practice, of antiemetics used for the control of chemotherapy induced emesis

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Emesis represents a major obstacle to cancer chemotherapy. To improve the control of emesis, serotonin antagonists, such as ondansetron, have been recently developed. These agents are considered more effective but more expensive than the traditional, metoclopramide based, antiemetic regimens. Objectives : The purpose of this study was to measure, in a context of current practice, the economic and quality of life impact of ondansetron based regimens, compared to metoclopramide based regimens in moderately emetogenic chemotherapy.
Methods: Female patients with breast cancer, naive to chemotherapy, scheduled to receive a cyclophosphamide based chemotherapeutic regimen (FAC, FEC or CNOE) were eligible for this prospective study. They received either an ondansetron or a metoclopramide based antiemetic regimen. The selection of the regimen was left to the physician to represent current practice. Because patients were naive, selection did not rest on predisposition to emesis, but depended upon access to treatment. Incidence of vomiting was recorded daily, in a patient diary, for five days following chemotherapy. Efficacy was measured in terms of complete control (0 vomiting episode) and major control (two or less vomiting episodes) a) during the first day and b) for the 5 day period immediately following chemotherapy. Quality of life was measured with the EORTC QLQ-C30 on three occasions : before the chemotherapy, 24 hours after and 72 hours after the chemotherapy. Costs related to emesis (medications, devices, pharmacy and nursing time), were collected for a 5 day period.
Results: Results for forty-nine patients (22 metoclopramide and 27 ondansetron) have been analyzed. Emesis control was significantly better in the ondansetron group: 74% had complete control the first day and 74% for the 5 day period compared to 32% (p=.004) and 27% (p=.002) respectively for metoclopramide. Major control was also superior with ondansetron at 93% for the first day and 85% for the 5 day period compared to 55% (p=.003) and 50% (p=.012) respectively with metoclopramide. Global quality of life decreased more substantially with metoclopramide than with ondansetron, but the difference did not reach statistical significance. For the 5 day period, average cost with ondansetron was higher than with metoclopramide, $103 vs. $70, but the cost effectiveness ratio for complete control was better with ondansetron,

$139 vs. $257. The incremental cost per additional patient with complete control was $70.78.
Discussion: Contrary to most other studies focussing on efficacy, this study provides effectiveness data, which reflects more closely the impact of treatments in current practice. This analysis of antiemetic treatments in the context of current practice would support the use of ondansetron for the control of emesis in breast cancer patients receiving a moderately emetogenic chemotherapy, as long as complete emesis control for a patient is valued at $70.78 or more.

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OP17. Costs and quality of life in metastatic colorectal cancer

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Background: Colorectal cancer is one of the most frequent solid tumors with an incidence rate of 150,000 cases per year in the United States and of 140,000 cases in Europe. Every year, 26,000 new cases were observed in France. One French people out of 25 is supposed to be affected by this disease. From a prevalence point of view, 47,000 colorectal cancer are managed every year by the French health care system, 40% to 50% of them will become metastatic.
Methods: A Markov process model was designed to assess the cost-utility of two associations: irinotecan + 5-FU and oxaliplatine + 5-FU, in advanced or metastatic colorectal cancer. The cohort was followed-up from the beginning of the chemotherapy until death. Markov states were defined according to the response status, and tolls were used to take into account toxicities. Transitional probabilities were calculated using actuarial method and density function approach. In the early stages of a development of new associations, it is very important to test the sensitivity of the cost-effectiveness ratio to change the various parameters. This analysis must be done with reference to the available treatment options. We used as a baseline for irinotecan + 5-FU, the results of 4 phase II trials in monotherapy, in a second-line metastatic colorectal treatment. We used as a baseline for oxaliplatine + 5-FU, a meta-analysis which synthetized the results of 7 clinical trials, in a second-line colorectal treatment. Finally, we simulated various assumptions on efficacy and safety to find out the cost-effectiveness of the new treatment regimens with alternative profiles of clinical outcomes and economic values. The Health Utility Index was used as a canevas to build the health states, which content validity was assessed by 2 medical specialists and 3 oncologic nurses. Health state preferences were measured through patients and experts opinions. To obtain a direct evaluation of the patients' preferences, the standard gamble and the feeling thermomether methods were tested on 20 patients. In the same time, interviews were made in order to define the experts' opinion. Costs were estimated, in the public and private sector, according to four points of view: the hospital pharmacists, the hospital heads of oncologic ward, the hospital managers and the health care system. Non medical direct and undirect costs were excluded from the calculation. In both public and private sectors, six units of valuation were tested: cost attributable to the patient, cost attributable to the ward, controlled cost by the ward, per diem cost, per diem tariff and DRG cost (ISA value and analytical accounting value).
Results: Quality of life coefficients varied according to the points of view. Compared to medical doctors, the patients gave higher quality of life values for health states with toxicity in the beginning of chemotherapy (except for nausea/vomiting and for neutropenia combined with diarrhea). When the toxicity was combined with objective response or stabilisation, quality of life assessment by the patients was lower than for the medical doctors. Incremental cost-effectiveness ranking remained unchanged whatever the point of view retained. On the contrary, the incremental cost-effectiveness ratio and the dominant strategy changed according to the unit of valuation chosen to calculate the cost of hospital resources utilisation.
Discussion: The cost of a therapeutic strategy does not exist in itself. There are as many definitions of cost as possible utilisations, and to obtain credible results 4 characteristics have to be defined before valuation: the costing object, its purpose, its content and the moment when it is calculated.

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OP18. Optimization of peripheral blood stem cell collection (PBSC) by leukapheresis: a case of interaction between economic and clinical assessment of an innovation

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Background : Using the example of substitution of peripheral blood stem cells collection to bone marrow (BM) harvest for autologous transplantation in cancer patients, our study try to illustrate the potential and limits of economic assessment starting at an early stage of medical innovation when major uncertainties still exist about the technology itself as well as its future diffusion.
Methods: We performed a cost-minimization study comparing the classical BM harvest with the initial PBSC collection protocol (3 systematic leukaphereses). We then compared these costs with those of an iterative protocol in which the number of leukapheresis sessions is not a priori decided, but rather in which leukaphereses are performed until a predetermined number of progenitors (measured by the number of CD34+ cells) has been collected. All patients were collected at the Institut Paoli-Calmettes between January 1992 and April 1994 for autograft. Direct medical costs of the procedures were estimated by measuring physical quantifies (capital and labor) arising from detailed observation carried out at the Institut Paoli-Calmettes.
Results: The average cost per patient of the BM harvest is of 4146$, and of the 3 systematic leukaphereses collection is of 5113$, i.e. 19% more costly than BM harvest. The cost comparison of an iterative PBSC procedure vs BM harvest is depending on the CD34+ threshold: PBPC is less costly if collection of $2x10^6$/kg CD34+ is considered to be sufficient for clinical reinfusion targeted, but becomes more costly if the minimum threshold for CD34+ is higher. Simulation of the iterative procedure shows the major influence of the CD34+ threshold on the PBSC collection average cost per patient, which varies from $2780 (with a threshold of $0.0.5x10^6$/kg CD34+) to $6700 (with a threshold of $10x10^6$/kg CD34+).
Discussion : One consequence of our study was to demonstrate that an iterative collection protocol (stopping leukaphereses sessions as soon as the threshold is reached) was an efficient way of minimizing cost. Following the study, the initial protocol at our institution (a priori planning of 3 leukaphereses session for all patients) was modified, and an iterative procedure was adopted (CD34+ are measured after each leukapheresis and a new session is only initiated if the $3x10^6$ /kg CD34+ threshold has not been reached). Finally the case of PBSC suggests that ongoing economic evaluation starting as early as possible throughout the "Research & Development" process can help predict subsequent diffusion of the technology over time, and potentiel evolution in expected clinical utilisation and costs.

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