external data using Bayesian MCMC methods. Economic analysis was undertaken using 1) standard cost-utility decision rules within each topic, and 2) constrained optimization rules across modelled topics. RESULTS: The guideline included fifteen individual economic evaluation topics. Under usual processes, piecewise economic modelling would have been used to evaluate between one and three guideline topics. The Whole Disease Model provided a consistent platform for the economic evaluation of eleven of the fifteen guideline topics, ranging from alternative diagnostic technologies through to cytotoxic treatments for metastatic disease. The constrained optimisation analysis identified a configuration of colorectal services which was expected to maximise QALY gains without exceeding current expenditure levels. CONCLUSIONS: This study evaluated the risk of Cancer incidence among patients with a diagnosis of DM compared with those without this pathology, in patients who had no reported history of Cancer at the start of the follow-up on January 2006. For the DM group, patients with at least one diagnosis of DM and a GP contact from January - December 2005 were selected, while for the DM-free group, patients with no diagnosis of DM and a contact with the GPs in the same period have been selected. Both groups have been followed-up for 5 years. In order to evaluate the association between the presence of DM and the incidence of Cancer multivariate logistic models, adjusted by age and sex have been implemented. RESULTS: A total of 73,144 (6 %) patients with a diagnosis of DM and 1,119,652 (94%) patients without DM diagnosis were selected. During follow-up 8,824 and 82,477 incident cases of Cancer were documented from the DM and DM-free groups respectively. Case-control analysis showed an Adjusted (age and sex) Odds Ratio of 1.06 (95% CI 1.06-1.20) suggesting that patients with DM have a 6% increased risk of Cancer incidence (all types). Regarding type-specific cancer analysis the OR for Liver cancer (2.44 [95% CI 2.11-2.82]) and Pancreas cancer (2.27 [95% CI 1.95-2.66]) were higher for DM patients. Patients with sex-specific cancers, the risk of Uterine body cancer was higher for DM patients (2.11-2.82) and Pancreas cancer (2.27 [95% CI 1.95-2.66]) were higher for DM patients. RESULTS: This study demonstrated that Whole Disease Model puts of the model are close to values observed in a real population. The purpose of this work was to calibrate an existing model for cervical cancer using Irish data and existing data to crossimulate model for cervical disease which was coded in C was embedded in a Bayesian framework. This is compared and contrasted with a previous random search calibration. METHODS: An existing microsimulation model for cervical disease which was coded in C was embedded in a loop running in R. MCMC, which is an iterative algorithm was implemented in parallel on multiple desktop machines and the results were collated for analysis. The calibration method used differs from pure optimisation strategies and identifies a probability distribution on the parameter space, which is of benefit for models requiring probabilistic sensitivity analysis. RESULTS: Estimates of the model parameter set were obtained from both MCMC and from the fitting of existing reference parameter sets resulting from a random search of the parameter space. These are compared on the basis of goodness of fit statistics (the sum of squared errors between targets and fitted values). Of 20 MCMC chains that were run, 5 of them gave better fits than the best fit sets for the random search method. However, of the 20 chains had not reached parameter sets that gave good fits when compared with the best 135 fitted sets from the random search method. CONCLUSIONS: MCMC is a useful technique which provides probabilistic estimates of the parameters of interest in a calibration exercise. Care is needed with starting values and proposal distributions, in order to ensure that the chains have converged and that the parameter space is properly explored.

OBJECTIVES: The treatment of breast cancer is associated with high costs, influenced by the introduction of more effective but expensive drugs, such as trastuzumab. This study aims to identify the new factors associated with the ageing of breast cancer in the adjuvant setting of early breast cancer and to explore the relation between (methodological) differences in study design and cost-effectiveness outcomes. METHODS: A systematic review was performed to identify cost-effectiveness studies of trastuzumab published between January 1998 and March 2011. All costs were converted to 2009 Euros. Sources of variation in study design were identified and divided into three categories: 1) methodological factors prescribed by national guidelines; and 2) intrinsic factors, such as methodological or practical choices made by the principal researchers; 3) extrinsic factors, such as the price of trastuzumab. RESULTS: Fourteen cost-effectiveness studies were identified in which one was a meta-analysis integrating data of multiple clinical trials. All were modelling studies. ICERs of chemotherapy + trastuzumab vs. chemotherapy alone ranged from being the dominant strategy to € 87,889/QALY gained. The level of detail provided regarding the design and usefulness of the study underpinning the identification of factors influencing this wide range of outcomes. However, of the mutually presented aspects, especially the treatment regimen of the underlying clinical trial seemed to influence outcomes. Variation among studies using the clinical trial appeared related to methodological factors prescribed by national guidelines, such as perspective and time horizon, intrinsic factors, such as assumed duration of benefit and extrinsic factors, e.g. country specific practice variation. CONCLUSIONS: Cost-effectiveness analysis of trastuzumab differed strongly, even between modelling studies based on the same clinical trial. Outcome was influenced by methodological aspects such as analysis perspective and time horizon assumed duration of benefit. A higher level of detail presented in the articles is needed to increase insight in causes of variation in cost-effectiveness outcomes.