Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study examined the cost-effectiveness of adding rituximab to the commonly used chemotherapy regimens as a first-line treatment for patients with advanced follicular non-Hodgkin’s lymphoma. The authors concluded that the addition of rituximab to these chemotherapy regimens was highly cost-effective from the UK National Health Service perspective. The study was well conducted and the assumptions required for the model were clearly reported and tested in the sensitivity analyses. The authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study examined the cost-effectiveness of adding rituximab to the commonly used chemotherapy regimens, as a first-line treatment for patients with advanced follicular non-Hodgkin’s lymphoma.

Interventions
The chemotherapy regimens were: mitoxantrone, chlorambucil, and prednisolone (MCP); cyclophosphamide, vincristine, and prednisolone (CVP); cyclophosphamide, doxorubicin (hydroxydaunorubicin), vincristine (Oncovin), and prednisolone (CHOP); and cyclophosphamide, doxorubicin, etoposide (VePesid), prednisolone (CHVP), and interferon alpha. Rituximab was added to each of these regimens. Patients treated with MCP or CVP, with or without rituximab, received eight cycles of treatment, while those receiving CHOP or CHVP, with or without rituximab, received six cycles of treatment, with interferon alpha given to those patients on CHVP for 18 months.

Location/setting
UK/hospital.

Methods
Analytical approach:
The economic evaluation was based on a Markov model with a lifetime perspective. The authors stated that the perspective of the UK National Health Service (NHS) was adopted.

Effectiveness data:
The clinical data were from four phase III randomised controlled trials (RCTs) that were carried out to provide up-to-date evidence for the change in the licence for rituximab. Each RCT compared rituximab plus one of the four chemotherapy regimens (MCP, CVP, CHOP, or CHVP plus interferon alpha) against that chemotherapy regimen alone. After the RCT follow-up period, patients in the rituximab treatment arm were assumed to have the same risk of disease progression as those in the chemotherapy only arm. Survival curves were used to project the long-term outcomes, from the RCT data. Life expectancy was based on official statistics, as there was low mortality in the RCTs. The monthly probability of disease progression was the key input to the model.

Monetary benefit and utility valuations:
The utility values were from a published study of 222 UK patients with follicular non-Hodgkin’s lymphoma. The European Quality of life (EQ-5D) questionnaire was used.
Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years (LYs) were the summary benefit measures and they were discounted at an annual rate of 3.5%.

Cost data:
The economic analysis included the costs of first-line medication (acquisition and administration), the costs of drugs in the progressed health state, and the costs of routine management or surveillance (out-patient visits). The resource consumption was from the RCTs and published literature. The unit costs for drugs were from the Monthly Index of Medical Specialties and the remaining costs were NHS reference costs. All costs were in UK pounds sterling (£) and future costs were discounted at a rate of 3.5% per annum. The price year was 2008.

Analysis of uncertainty:
Univariate sensitivity analyses were carried out on a range of parameters, including the utility values, rate of disease progression, time horizon, and cost of medication and monitoring. The sources of alternative estimates were published studies or authors’ opinions. A probabilistic sensitivity analysis, based on a second-order Monte Carlo simulation, was undertaken using predetermined probability distributions for the model inputs.

Results
The addition of rituximab increased the costs by £8,826 with MCP, £7,874 with CVP, £8,872 with CHOP, and £3,892 with CHVP. The gain in QALYs was 1.184 with MCP, 0.914 with CVP, 0.831 with CHOP, 0.458 and with CHVP. The gain in LYs was 1.357 with MCP, 1.054 with CVP, 0.955 with CHOP, and 0.528 with CHVP.

The incremental cost with rituximab was £7,455 per QALY or £6,503 per LY gained with MCP, £8,613 per QALY or £7,473 per LY gained with CVP, £10,676 per QALY or £9,294 per LY gained with CHOP, and £8,498 per QALY or £7,370 per LY gained with CHVP.

The most influential input to the model was the time horizon; with a shorter time horizon, the results for the rituximab arm were less favourable. The probabilistic analysis confirmed that the addition of rituximab was very likely to be cost-effective, at a willingness-to-pay threshold of £20,000 per QALY.

When all treatments were compared, a cost-effectiveness league table was developed to assess which first-line treatment was the most cost-effective. Excluding dominated strategies, which were less effective and more expensive than another option, the incremental cost per QALY gained was £235 with MCP over CVP, and £7,454 with rituximab plus MCP over MCP alone. In general, rituximab plus MCP was the preferred option, when they were all compared, across the chemotherapy regimens.

Authors’ conclusions
The authors concluded that the addition of rituximab to the chemotherapy regimens was highly cost-effective from the UK NHS perspective.

CRD commentary
Interventions:
The selection of the comparators was appropriate, as they were the chemotherapy regimens that were most commonly used for the treatment of follicular lymphoma, in the UK.

Effectiveness/benefits:
The clinical data came from selected sources. The RCTs were chosen because they were the pivotal trials for the new use for rituximab. Each trial provided data on rituximab compared with the chemotherapy regimen alone. RCTs are usually considered to be valid sources of evidence, given their methodological strengths. The details of these trials were published elsewhere. Appropriate survival curves were used to project the short-term data to the patient's lifetime. Some assumptions were also needed, but these were extensively investigated in the sensitivity analysis. Both the benefit measures were appropriate as they capture the impact of the interventions on a patient's health. The utility values, used to calculate the QALYs, were appropriately from a UK study that used a validated instrument.
Costs:
Both the cost categories and the sources for the unit costs were consistent with the perspective adopted. A list of cost items was provided for most categories and some unit costs and quantities of resources were reported. The impact of variations in the key costs was tested in the sensitivity analysis. The economic analysis was generally well carried out and presented. Details, such as the price year and discount rate, were provided.

Analysis and results:
The results were appropriately synthesised, using an incremental approach, and they were clearly presented. The uncertainty was satisfactorily investigated and the results were extensively presented and discussed. Conventional discounting was applied to both the costs and benefits. The Markov model had been published elsewhere and correctly described the disease progression. The data analysed were representative of the UK situation, but it was not clear whether they were transferable to other settings.

Concluding remarks:
The study was well conducted and the assumptions required for the model were clearly reported and tested in the sensitivity analyses. The authors’ conclusions appear to be robust.

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