Quality of life and cost-effectiveness of interferon-alpha in malignant melanoma: results from randomised trial
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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.

Health technology
Patients with thick primary cutaneous melanoma were given interferon (IFN) alpha-2a at 3 mega units (MU) three times a week for 2 years or until recurrence. The comparator treatment was to be given no further treatment.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients with thick primary cutaneous melanoma who were eligible to receive IFN and who met the inclusion criteria set down in the earlier effectiveness paper (Hancock et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic details).

Setting
The setting was secondary care. The economic study was carried out in the UK.

Dates to which data relate
The dates to which the effectiveness evidence referred were not given in this paper (see Hancock et al. 2004). Dates for the resource evidence were also not given. The price year was 2003 to 2004.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
A sub-set of patients providing the effectiveness data also provided the cost data. The cost data were collected prospectively.

Study sample
Details of power calculations and sample selection were given elsewhere (Hancock et al. 2004). There were 338 patients in the IFN-alpha group and 336 in the observation alone (OBS) group.

Study design
This was a multi-centred randomised controlled trial (RCT). Patients were intended to be followed up for up to 5 years, but some patients were followed up for 77 months. There were follow-up data for 211 (68%) patients in the IFN-alpha group and 187 (56%) patients in the OBS group.

**Analysis of effectiveness**
The analysis was conducted on an intention to treat basis. The primary health outcomes used were the scores from the EORTC-QLQ-C30 V1 function and symptom scale scores, and quality-adjusted life-years (QALYs). The two patient groups were similar at baseline in their demographics and in their EORTC QLQ-C30 function and symptom scores.

**Effectiveness results**
The difference in mean EORTC-QLQ-C30 V1 function scores at follow-up (i.e. OBS score minus IFN score, after adjustment for baseline score and overall survival status) was:

2.1 (95% confidence interval, CI: -0.7 to 4.5; p=0.144) for physical functioning;

4.3 (95% CI: 0.4 to 8.3; p=0.033) for role functioning;

4.5 (95% CI: 1.6 to 7.4; p=0.003) for emotional functioning;

4.1 (95% CI: 1.8 to 6.4; p=0.001) for cognitive functioning;

4.4 (95% CI: 1.5 to 7.3; p=0.003) for social functioning; and

5.9 (95% CI: 3.1 to 8.7; p=0.001), for global health status.

The difference in mean follow-up symptom score (i.e. OBS score minus IFN score), where a higher score means a worse outcome, was:

-9.1 (95% CI: -12.1 to 6.1; p=0.001) for fatigue;

-3.4 (95% CI: -5.3 to -1.6; p=0.001) for nausea and vomiting;

-0.1 (95% CI: -3.4 to 3.1; p=0.937) for pain;

-3.7 (95% CI: -6.5 to -0.9; p=0.010) for dyspnoea;

-3.2 (95% CI: -7.2 to 0.9; p=0.123) for insomnia;

-6.2 (95% CI: -9.5 to -3.0; p=0.001) for appetite loss;

-3.3 (95% CI: -5.8 to -0.7; p=0.011) for constipation;

-4.4 (95% CI: -6.9 to -2.0; p=0.001) for diarrhoea; and

-4.7 (95% CI: -7.4 to -2.0; p=0.001) for financial difficulties.

**Clinical conclusions**
The authors concluded that the symptoms of patients taking IFN were worse than those of patients taking placebo. Therefore, IFN could be recommended only if the QALY analysis showed that the better life expectancy outweighed the worse quality of life.

**Modelling**
The Kaplan-Meier method was used to calculate the time from randomisation to death.
Measure of benefits used in the economic analysis
The measure of benefits used was the QALYs. Health states were valued through EQ-5D scores, using UK population values and combining them with mortality data, as described in Drummond et al. 1997, (see ‘Other Publications of Related Interest’ below for bibliographic details). Baseline EQ-5D values were missing, so these were imputed by regressing the EORTC QLQ-C30 on EQ-5D values from other visits.

Direct costs
The costs incurred after one year were discounted at a rate of 3.5% per annum. The quantities and the costs were not analysed separately. The costs of IFN, inpatient and outpatient hospital care, community nurse care and general practitioner care were measured. The resource data came from the study case report form and patient questionnaire. The prices came from the British Medical Association 2002 and Netten and Curtis 2003, (see ‘Other Publications of Related Interest’ below for bibliographic details). The price year was 2003 to 2004.

Statistical analysis of costs
Independent sample t-tests were performed on cost differences and p-values were reported.

Indirect Costs
No indirect costs were calculated.

Currency
UK pounds sterling ().

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
After 5 years, the QALY analysis which used the EQ-5D scores showed that the total QALYs were 2.40 (standard deviation, SD=1.19) in the IFN group and 2.33 (SD=1.25) in the OBS group, (p=0.752).

A total of 0.074 QALYs per person were gained as a result of using IFN. Side effects of treatment were also considered. The benefits were calculated for 5 years.

Cost results
The total costs were displayed graphically and were 3,066 higher in the IFN group than in the OBS group, (p=0.396). The costs of adverse effects were dealt with in the costing.

Synthesis of costs and benefits
The incremental cost per QALY gained was 41,432.

There was a 45% chance that the cost per QALY would be no more than 30,000.

Authors’ conclusions
Given the high estimated cost per quality-adjusted life-year (QALY) of 41,432, and the statistical uncertainty surrounding this estimate, low-dose extended-duration interferon (IFN) therapy for melanoma patients does not appear
to be a wise use of resources in the UK.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparator, no further treatment and continued observation of the patient, was justified by it being current practice in many settings. You should decide if it represents current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The source of the effectiveness data was a single study. The study design, an RCT, was appropriate for the hypothesis. The study sample was representative of the study population and the patient groups were shown to be comparable at analysis. The analysis of effectiveness was handled credibly, but it would have been useful to have seen the results of the EQ-5D questionnaires as these provided the information necessary for the calculation of the QALYs. No other sources were used for the effectiveness data.

**Validity of estimate of measure of benefit**
The authors adequately reported the methods used for deriving the QALYs. The measure of benefit, QALYs, has the potential to capture the full range of health benefits. The authors noted that the cost-effectiveness results were derived from data up to 5 years after treatment. It is possible that, with data collected over a longer time period, the results could have been different.

**Validity of estimate of costs**
From the cost perspective adopted, all the relevant categories of costs appear to have been included in the analysis. However, the authors did not itemise all the costs. The costs were not reported separately from the quantities. The resource use quantities were taken from a single study, while the unit costs were taken from published sources. The price year was reported.

**Other issues**
The authors made appropriate comparisons of their results with the findings from other studies. The issue of generalisability to other settings was not discussed. The authors devoted a lot of the article to the EORTC-QLQ-C30 V1 results and did not present the EQ-5D results, which seems strange as the EQ-5D results were the ones they used to calculate the benefits. The authors' conclusions reflected the scope of the analysis. The authors noted that the economic data only related to a sub-sample of 111 patients and it would have been better to have had data on a higher percentage of patients. The authors pointed out that only 66% of the patients had a baseline EORTC assessment, and that the number and timing of quality of life assessments varied between patients. Thus, a summary measure of quality of life based on average scores was used.

**Implications of the study**
The authors concluded that, in the UK, their study does not show sufficient benefit to justify the expenditure of low-dose extended-duration adjuvant IFN-alpha therapy for patients with malignant melanoma, as the cost per QALY gained was more than 41,000.

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**Bibliographic details**
Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Antineoplastic Agents /economics /therapeutic use; Cost-Benefit Analysis; Dose-Response Relationship, Drug; Female; Health Care Costs /statistics & numerical data; Humans; Interferon-alpha /economics /therapeutic use; Male; Melanoma /drug therapy /economics; Middle Aged; Placebos; Quality of Life; Quality-Adjusted Life Years; Skin Neoplasms /drug therapy /economics; Survival Analysis

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