Testing women with endometrial cancer to detect Lynch syndrome
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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.

CRD summary
This study examined the cost-effectiveness of various criteria to determine who to test to identify Lynch syndrome in women with endometrial cancer, to prevent colorectal cancer. Immunohistochemistry triage for women with at least one first-degree relative with a Lynch syndrome-associated cancer at any age was cost-effective. The Amsterdam II criteria missed a large percentage of affected women. The cost-effectiveness framework was conventional and appropriate, and the authors’ conclusions appear to be robust, but limited information on the data sources was given.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of various testing criteria to identify Lynch syndrome in women with endometrial cancer, in order to prevent colorectal cancer.

Interventions
The following six sets of criteria to identify patients to be tested were considered: Amsterdam II criteria; younger than 50 years old with at least one first-degree relative diagnosed with Lynch syndrome-associated cancer at any age; immunohistochemistry (IHC) triage for those under 50 years old; IHC triage for those under 60 years old; IHC triage at any age for those with one diagnosed first-degree relative; and IHC triage of all women with endometrial cancer.

The Amsterdam II criteria were at least two relatives diagnosed with Lynch syndrome-associated cancer, within two successive generations, with at least one relative diagnosed before the age of 50 years.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The analysis was based on a Markov model, with a lifetime horizon. The authors stated that it was carried out from the perspective of society.

Effectiveness data:
The clinical data were from a selection of relevant studies. Some of the data on the proportion of endometrial cancer detected were from the Surveillance, Epidemiology, and End Results (SEER) database, from 1988 to 2001. The sensitivity and specificity of the Amsterdam II criteria and IHC were the primary inputs for the clinical analysis.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
Life-years were the summary benefit measure and they were discounted at an annual rate of 3%.

Cost data:
The economic analysis included the costs of IHC, genetic counselling, deoxyribonucleic acid (DNA) sequencing.
colonoscopy, and the long-term treatment of colorectal cancer. The costs of colorectal cancer treatment were from published literature, while other data were from Medicare. All costs were in US dollars ($) and a 3% annual discount rate was applied. The price year was 2010.

Analysis of uncertainty:
One- and two-way sensitivity analyses were carried out to assess the uncertainty around model inputs. Alternative values were from published sources or authors' opinions. A Monte Carlo simulation was carried out, using tracker variables within the Markov model to estimate the number of women who would be identified as having Lynch syndrome, and the subsequent number of colorectal cancer cases.

Results
The average costs were $2,254 for testing those under 50 years old with one diagnosed first-degree relative, $2,255 for IHC triage for those under 50 years old, $2,277 for IHC triage for those with one diagnosed first-degree relative, $2,484 for IHC triage for those under 60 years old, $3,131 for IHC triage for all patients, and $4,045 for the Amsterdam II criteria.

The life-years were 14.52708 for those under 50 years old with one diagnosed first-degree relative, 14.52686 for IHC triage for those under 50 years old, 14.52971 for IHC triage for those with one diagnosed first-degree relative, 14.52792 for IHC triage for those under 60 years old, 14.53077 for IHC triage for all patients, and 14.52733 for the Amsterdam II criteria.

After excluding the dominated strategies, which were less effective and more expensive than another strategy, compared with testing those under 50 years old with one diagnosed first-degree relative, the incremental cost per life-year gained was $9,126 with IHC triage for those with one first-degree relative, and $648,494 with IHC triage for all patients, compared with those with one first-degree relative. At a cost-effectiveness threshold of $50,000 per life-year gained, IHC triage for those with one diagnosed first-degree relative was the preferred strategy.

The sensitivity analysis showed that the base-case findings were robust to variations in both the clinical and economic inputs. The Amsterdam II criteria strategy was dominated unless its specificity and sensitivity were over 95%.

Authors' conclusions
The authors concluded that IHC triage for women with endometrial cancer, who had at least one first-degree relative with a Lynch syndrome-associated cancer at any age, was cost-effective. The Amsterdam II criteria missed a large percentage of affected women.

CRD commentary
Interventions:
A wide range of possible interventions was appropriately considered and they are likely to be valid for other health care systems. The Amsterdam II criteria were the recommended strategy in the USA.

Effectiveness/benefits:
Limited information on the sources of clinical data was provided. In general, the clinical inputs were from published studies or standard US databases, but the details were not given and it is not possible to judge the validity of the clinical data. The authors stated that high uncertainty was found in the published studies and extensive sensitivity analysis was conducted. Life expectancy was a relevant benefit measure for women with cancer, but it is not clear why quality of life was not included.

Costs:
The authors stated that a societal perspective was adopted, but the categories of costs reflected a third-party payer perspective. The unit costs and resource quantities were not presented separately and costs were reported as category totals, as often occurs when Medicare tariffs are used. Little information on the published sources for the estimate of long-term colorectal cancer costs was provided. The costs were varied in the sensitivity analysis. Other details, such as the price year and discount rate, were appropriately reported.
Analysis and results:
The results were extensively presented. An appropriate incremental approach was used to synthesise the costs and benefits of the alternative strategies, excluding the dominated ones. The uncertainty was investigated, using deterministic and probabilistic approaches, but the findings were selectively presented. The analysis was specific to the US context and the authors did not discuss the transferability of their results. The main finding was that the Amsterdam II criteria were very unlikely to be cost-effective in the USA.

Concluding remarks:
The cost-effectiveness framework was conventional and appropriate, and the authors' conclusions appear to be robust, but limited information on the data sources was given.

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