Management of incidental pituitary microadenomas: a cost-effectiveness analysis

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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
Use of one of four strategies in the management of patients with an incidentally discovered asymptomatic pituitary microadenoma. The four strategies considered were as follows: (1) expectant management; (2) prolactin (PRL) screening; (3) a panel of hormone screening tests (PRL, insulin-like growth factor I (IGF-I), and 1 mg dexamethasone suppression of cortisol), and; (4) follow-up magnetic resonance imaging (MRI) screening. Any abnormal cases discovered were referred for treatment by the appropriate pharmacological (bromocriptine) or surgical treatment.

Type of intervention
Screening, diagnosis, and treatment.

Economic study type
Cost-utility analysis.

Study population
Patients with an incidentally discovered asymptomatic pituitary microadenoma.

Setting
Hospital. The economic study was carried out in the USA.

Dates to which data relate
Effectiveness data were obtained from studies published between 1978 and 1996. The resource use data and corresponding dates were not reported. The fiscal year was 1995.

Source of effectiveness data
Effectiveness data were derived from a review of the literature and the clinical judgement of a panel of experts.

Modelling
The incremental cost-effectiveness ratios were estimated based on a decision analytic Markov model.

Outcomes assessed in the review
The following outcomes were assessed:

- Probability of a positive test with MRI (annual incidental microadenoma growth rate);
- probability of a positive test with endocrine (patient with neurologic symptoms from pituitary mass) with PRL;
- incidence of pituitary disease including prolactinoma, acromegaly, and Cushing's syndrome;
outcome from pituitary surgery of macroadenoma including failure to relieve symptoms, neurological deficit, and death;

outcome from pituitary surgery of microadenoma including failure to relieve symptoms (of hyperprolactinemia, Cushing's syndrome, and acromegaly), neurological deficit, and death;

quality of life values for various health states including hyperprolactinemia, Cushing's syndrome, acromegaly, bromocriptine treatment, incidental microadenoma (after 2 years), incidental microadenoma (first 2 years), and stroke or neurological deficit;

and relative risk of death for acromegaly, and Cushing's syndrome.

The test characteristics (sensitivity, specificity, accuracy) and effectiveness of bromocriptine were discussed.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
A total of 16 papers were directly referred to as sources of clinical probabilities incorporated in the model. An extra set of 16 papers was referred to in the discussion on the test characteristics and effectiveness of bromocriptine.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The outcome results (range for sensitivity analyses) were as follows:

probability of a positive test with MRI (annual incidental microadenoma growth rate), 0.017 (0.0017-0.17);

probability of a positive test with endocrine (patient with neurologic symptoms from pituitary mass) with PRL, 0.40;

incidence of pituitary disease including prolactinoma, 0.000026 (1-100X baseline), acromegaly, 0.000003 (1-100X baseline), and Cushing's syndrome, 0.0000024 (1-100X baseline);

outcome from pituitary surgery of macroadenoma including failure to relieve symptoms, 0.25 (0.05-0.75), neurological deficit, 0.027 (0.005-0.125), and death 0.0086 (0.0013-0.04);
outcome from pituitary surgery of microadenoma including failure to relieve symptoms of hyperprolactinemia, 0.20 (0.05-0.4), Cushing's syndrome, 0.15 (0.05-0.3), acromegaly, 0.16 (0.05-0.3), neurological deficit, 0.004 (0.001-0.02), and death, 0.0027 (0.005-0.125);

quality of life values for various health states including hyperprolactinemia, 1.00 (0.9-1.00), Cushing's syndrome, 1.00 (0.9-1.00), acromegaly, 1.00 (0.9-1.00), bromocriptine treatment, 1.00 (0.9-1.00), incidental microadenoma (after 2 years), 1.00, incidental microadenoma (first 2 years), 0.99 (0.90-0.99), and stroke or neurological deficit, 0.75 (0.74-0.77);

relative risk of death for acromegaly, 2.01 (1.00-2.01), and Cushing's syndrome, 3.84 (1.00-3.84).

It was reported that the data on test characteristics (sensitivity, specificity, accuracy) and effectiveness of bromocriptine for patients with incidental asymptomatic pituitary microadenoma were not readily available. Further details on probabilities are provided in the paper.

**Methods used to derive estimates of effectiveness**
Clinical judgement (consensus of four physicians, of whom two were endocrinologists) was also used to derive estimates of effectiveness.

**Estimates of effectiveness and key assumptions**
The outcome results were as follows:

Patients with positive endocrinological symptoms: clinical probability of positive initial PRL test, 0.05 (0.01 - 0.05), with confirmatory PRL test, 0.50 (0.05 - 0.99), with 1 mg dexamethasone suppression test, 0.05 (0.01 - 0.05), with confirmatory urinary free cortisol+ACTH, 0.25 (0.05 - 0.99), with initial IGF-I, 0.05 (0.01 - 0.05), with confirmatory IGF-I, 0.99 (0.05 - 0.99);

incidence of neurological symptoms from a pituitary mass, 0.000006 (0.1-100X baseline);

quality of life value for the health state of no endocrinopathies or neurological deficits, 1.00;

relative risk of death for hyperprolactinemia, 1.02 (1.00-1.02), and for bromocriptine, 1.01 (1.00-1.01).

**Measure of benefits used in the economic analysis**
The benefit measure was quality-adjusted life years (QALYs) for a time horizon of 10 years (range for sensitivity analyses, 2-50 years).

**Direct costs**
Costs were discounted for a time horizon of 10 years (range for sensitivity analyses, 2-50 years). Cost items were reported separately. Cost analysis covered the direct medical costs of drugs, tests, hospitalisation, physician fees, etc. The perspective adopted in the cost analysis was reported to be that of society. The sources of cost data were Medicare diagnostic related groups, Medicare physician fee schedules, and the Drug Topics Red Book, published between 1994 and 1995. The date of the price data was 1995.

**Indirect Costs**
Not considered.

**Currency**
US dollars ($).
Sensitivity analysis
A series of one-way and multi-way sensitivity analyses was conducted on all parameters of the model. Threshold values were calculated for sensitive inputs.

Estimated benefits used in the economic analysis
The total QALYs for the four strategies for a time frame of 10 years were: expectant management, 8.0417, PRL screening, 8.0654, endocrine panel, 8.0702, and follow-up MRI screening, 8.0604. The discount rate was 5%.

Cost results
The discount rate was 5%. The total costs for a time frame of 10 years were $24 for expectant management, $58 for PRL screening, $401 for endocrine panel, and $1,949 for follow-up MRI screening.

Synthesis of costs and benefits
The incremental cost per QALY was calculated as the measure of cost-effectiveness, leading to values of $1,428, and $69,495 for the strategies of PRL screening and endocrine panel, compared to the least effective and least costly strategy of expectant management. Either PRL screening or endocrine panel dominated the strategy of MRI follow-up. The sensitivity analyses established the relative robustness of the study results over a wide range of reasonable values for the model inputs. The most sensitive parameter was patient anxiety about microadenoma, which could swing the results in favour of the endocrine screening panel.

Authors' conclusions
The authors concluded that "in patients with an incidental asymptomatic pituitary microadenoma, a single PRL test may be the most cost-effective management strategy".

CRD COMMENTARY - Selection of comparators
No specific health technology was regarded as the comparator since it was reported that the current "recommendations for the management of incidental microadenomas are controversial" and the "limited available data suggest that clinical practice varies widely." You, as a database user, should therefore consider which health strategy is widely used in your own setting.

Validity of estimate of measure of benefit
The internal validity of the estimates of benefit measure can not be assessed due to lack of information regarding the comprehensiveness of the literature review, and the quality assessment of the primary studies included in the review.

Validity of estimate of costs
Adequate details of methods of cost estimation were given. Despite the societal perspective reportedly adopted in the cost analysis, indirect costs were not included. Cost results may not be generalisable to other settings or countries.

Other issues
Extensive sensitivity analyses were performed to handle the uncertainties surrounding the data and adequate comparisons were made with other studies.

Implications of the study
From the study results it can be implied that "Reassurance (removing the anxiety of patients) is not a trivial benefit; the sensitivity analysis demonstrates the importance of patient anxiety in determining the optimal management of an incidental microadenoma".
Source of funding
None stated.

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