Diagnosis and treatment of adrenal incidentaloma: 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
Several health technologies were considered for the diagnosis and the treatment of adrenal incidentaloma, an adrenal mass incidentally detected during the course of abdominal diagnostic imaging, performed for another reason. The eight diagnostic tests were grouped in three sets: imaging techniques, namely I-iodomethyl-norcholesterol (NP59), magnetic resonance imaging, I-meta-iodobenzylguanidine, and computed tomography; hormonal analyses (assessment of adrenocortical function and/or adrenomedullary function); and fine-needle aspiration cytology. The two treatment strategies were adrenalectomy by flank approach or transabdominal route, using either an open or laparoscopic technique.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients in whom an adrenal incidentaloma was detected.

Setting
The setting was community. The study was carried out in the Netherlands.

Dates to which data relate
The effectiveness evidence was gathered from studies published between 1974 and 1998. The dates during which resource use data were collected were not reported. The price year was 1998.

Source of effectiveness data
The effectiveness data were derived from a systematic review of published studies.

Modelling
A decision tree model was constructed in order to estimate the costs and effectiveness of each strategy in the study. The average age of patients in the model was 57.5 years, and approximately 61% of the patients were female.

Outcomes assessed in the review
The variables assessed in the review were subdivided into four categories:

the probabilities of underlying disorders, i.e. events which could cause adrenal incidentaloma;
signs, symptoms and clinical information, for example, incidentaloma diameter, hypertension and headache;

the sensitivity and specificity of diagnostic tests; and

the effectiveness of treatments, in terms of, for example, mortality, primary adrenocortical cancer.

These estimates were obtained from the literature and used as input parameters in the decision model.

**Study designs and other criteria for inclusion in the review**
Inclusion criteria for primary studies were not reported.

**Sources searched to identify primary studies**
Primary studies were identified through a 20-year search of MEDLINE, with examination of cross-references between articles.

**Criteria used to ensure the validity of primary studies**
The validity of primary studies was ensured by selecting articles that used unambiguous variable definitions, contained quantitative data to calculate variables, reported original data, and contained a minimum number of 10 observations per variable.

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

**Number of primary studies included**
Approximately 94 primary studies were included in the review.

**Methods of combining primary studies**
The primary studies were combined by a meta-analysis, using odds ratios and positive and negative likelihood ratios to aggregate the data. The diagnostic characteristics of the tests were combined using Mantel-Haenszel odds ratios and summary receiving operator characteristic curve methods. The probabilities, proportions, and real variables were aggregated using an inverse variance-weighted means technique.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
Numerous variable estimates were assessed in the review. The probability of underlying disorders was 0.835 for inactive benign cortical adenoma, 0.046 for primary adrenocortical cancer (PACC), 0.034 for pheochromocytoma, 0.055 for active benign cortical adenoma, 0.024 for metastasis, and 0.006 for Conn's syndrome.

The estimates of treatment outcomes were 0.017 for operative mortality, 0.830 for PACC operable, and 0.492 for PACC curatively resectable.

**Measure of benefits used in the economic analysis**
Quality-adjusted life-years (QALYs) or days were used as benefit measures in the economic analysis. Several intermediate outcomes were also considered. The future benefits were discounted at a rate of 3%.
Direct costs
A 3% discount rate was used for the cost estimations. Unit costs were primarily based on published US data. However, if these costs were unavailable, Dutch unit costs were determined from material, personnel and overhead costs, using data from the Leiden University Hospital Information System, and were then converted into US dollars. The costs and quantities were not reported separately. The expected total costs of each strategy were obtained through a decision model. The dates during which resource use data were collected were not reported. The price year was 1998.

Statistical analysis of costs
Not reported.

Indirect Costs
Indirect costs were determined from the number of days off work multiplied by the US per capita per day gross national product.

Currency
US dollars ($).

Sensitivity analysis
The authors undertook 2-way sensitivity analysis on the variables age and incidentaloma. Additionally, several variables were varied in the model to assess their impact on the economic analysis results; these included signs, symptoms, clinical information, age and gender.

Estimated benefits used in the economic analysis
The number of QALYs associated with each strategy was reported for two cases in the reference scenario, where only the presence and the diameter of the incidentaloma were known. The full hormone analysis produced more QALYs, both in the case of a patient with a 2.5 cm incidentaloma (15.69 QALYs), and a 6 cm incidentaloma (12.88 QALYs). However, the numbers of QALYs associated with the other strategies were also very close to the best option: the worst alternative produced 15.50 and 12.63 QALYs in the first (2.5 cm incidentaloma) and second (6 cm incidentaloma) cases, respectively.

Cost results
For a patient with a 2.5 or 6 cm incidentaloma, the least expensive strategy was the medullary hormone analysis; the total costs were $1,500 and $1,700, respectively. The next least expensive strategy was fine-needle aspiration cytology with total costs of $2,350 and $5,400, respectively. The expected total costs of the other strategies ranged quite widely, with the most expensive being the surgery option (without testing); this cost $19,950 and $20,000 in the two cases.

Synthesis of costs and benefits
The costs and benefits were combined by an incremental cost-effectiveness analysis. Given the high number of possible combinations of the strategies, only few cases were reported by the authors.

In the reference scenario, and with respect to single strategies, the most cost-effective strategy was the adrenomedullary hormonal analysis, with an incremental cost-effectiveness ratio of $22,400 per QALY compared with the next best alternative. This dominated the other strategies, with the exception of full hormonal analysis, which had an excessive incremental cost-effectiveness ratio of $1,366,100 per QALY.

In the same scenario and with respect to two-step strategies, the most cost-effective option was hormonal analysis and fine-needle aspiration cytology (0.11 QALYs at $30,150) when compared with ignoring the incidentaloma.
In a second scenario, where a preliminary diagnosis of the presence and kind of incidentaloma was based on either magnetic resonance imaging or computed tomography, the medullary hormone analysis was the preferred approach if the disease was benign (0.7 QALYs at $22,200).

Several other combinations of strategies were reported in the paper. The authors analysed the impact of some variables on the analysis results. They concluded that patient age and incidentaloma diameter had the highest impact on the preferred strategies.

Authors’ conclusions
The main conclusion was that the health risk of an adrenal incidentaloma depended primarily on patient characteristics and the incidentaloma. The diagnostic-therapeutic strategy chosen had far less impact. However, it seemed that the ignoring option and immediate surgery were rarely justified. Diagnostic testing was indicated for most patients and adrenal hormonal function offered the highest QALYs gains, with an analysis of adrenomedullary function being the best strategy for smaller incidentalomas and full hormonal analysis being preferred for those of at least 6 cm in diameter.

CRD COMMENTARY - Selection of comparators
The authors did not provide a justification for their selection of the strategies compared, but it seemed that they represented the current practice in clinical management of adrenal incidentalomas. You, as a database user, should consider whether they represent widely used technologies in your own setting.

Validity of estimate of measure of effectiveness
The principal input parameters for the model were derived from a well-conducted meta-analysis. However, the authors did not consider the impact of differences among the primary studies when estimating effectiveness. In addition, the authors acknowledged that study conclusions were adequate for categories of patients with specific characteristics.

Validity of estimate of measure of benefit
The benefit measure was based on the calculation of the total number of QALYs associated with each strategy, and was obtained through a decision model. However, the model structure was not reported; further details would have been useful to aid understanding of the study.

Validity of estimate of costs
Given that only expected total costs were reported in the paper, very few details of the direct and indirect costs were provided. The costs and quantities were not reported separately, and statistical analyses of resources and costs were not performed. Furthermore, the dates when resources and costs were gathered were not reported explicitly, and it was unclear how future costs due to extended life years were accounted for in the analysis.

Other issues
The authors did not address the issue of the generalisability of the study results to other settings, although the sensitivity analyses conducted at least partly addresses this issue. The analysis findings were similar to those reported in other papers. The authors indicate that the findings of this study have been updated and can be viewed on the Internet (see url's below).

Implications of the study
The authors recognised that, in clinical practice, choices are generally made on the basis of psychological and social mechanisms, such as certainty preferences and risk aversion. However, the study results should clearly help clinicians make decisions about the expected gains and losses of various choices for the management of adrenal incidentaloma. The authors suggest that further research should focus on prospective empirical evaluation of the disease, based on a
more individualised approach.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
10732265

**Original Paper URL**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adenoma /diagnosis /economics /therapy; Adrenal Gland Neoplasms /diagnosis /economics /therapy; Cost-Benefit Analysis; Female; Humans; MEDLINE; Male; Middle Aged; Treatment Outcome

**AccessionNumber**
22000000604

**Date bibliographic record published**
28/02/2002

**Date abstract record published**
28/02/2002