Prenatal screening for Down's syndrome using inhibin-A as a serum marker
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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
Inhibin-a serum marker with human chorionic gonadotrophin, alpha-fetoprotein (AFP), and unconjugated oestriol (uE3) used in prenatal screening for Down's syndrome.

Type of intervention
Primary prevention and screening.

Economic study type
Cost-effectiveness analysis.

Study population
Caucasian pregnant women.

Setting
Hospital. The economic study was carried out in London, UK.

Dates to which data relate
The dates associated with the collection of the main effectiveness data were not clearly stated (reported sources were dated 1988-92). The dates associated with the resource use data and the prices were not reported.

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

Link between effectiveness and cost data
The costing was performed retrospectively on a different patient sample than that used in the effectiveness study.

Study sample
Stored serum samples from 77 Down's syndrome singleton pregnancies and 385 unaffected singleton pregnancies, supplemented by data from 970 white women with unaffected pregnancies, were used in the study.

Study design
Case-control study. The duration of the follow-up was until after delivery.

Analysis of effectiveness
The primary outcome was that of cases detected for a given false positive rate (5%). The case (affected) and control (n=385) groups were matched for maternal age, gestational age, and duration of storage of the sample. The estimation of the risk of Down's syndrome pregnancy was derived from the woman's age (from data for the maternal age-specific risk of a Down's syndrome pregnancy using the rate in live births from a study published in 1987) and univariate or multivariate Gaussian distributions derived from the various combinations of the serum markers used. The truncation limits used in calculating such a risk were as follows: 0.3-3.3 multiples of the normal median for unaffected pregnancies of the same gestational age (MOM) for AFP; 0.5-2.0 MOM for uE3, 0.2-5.0 MOM for total hCG; 0.33-3.0 MOM for free Beta-hCG; 0.5-2.0 MOM for free Beta-hCG; and 0.4-3.5 MOM for inhibin-A.

**Effectiveness results**

The use of the intervention (inhibin-A based four marker test) instead of the comparator (alpha-hCG based four marker test) would yield a sensitivity (detection) rate, for a given false-positive rate of 5%, of 67% instead of the 65% of the alternative strategy. Similar results obtained if total hCG was used instead of the free beta-hCG. The use of ultrasound scan examination to estimate gestational age (rather than using dates as implicitly assumed by the previous estimates) would increase figure for the intervention to 76%. Maternal weight adjustment of inhibin-A were made.

**Clinical conclusions**

The risk cut-off level that would be required to achieve a particular screening performance will depend on local practice regarding the use of ultrasound to estimate gestational age and maternal weight adjustment. Centres that routinely do both can expect to detect 77% of Down's syndrome pregnancies with 5.2% false-positive rate by selecting a 1:300 risk cut-off level. This level of performance makes the inhibin-A-based four-marker test the most effective method of Down's syndromescreening currently available for routine use.

**Measure of benefits used in the economic analysis**

The measures of benefit were the cases of women with Down's syndrome pregnancies detected and the number of fetal losses through amniocentesis avoided.

**Direct costs**

The quantities of resource use were analysed separately from the costs. The costs measured were those associated with the diagnostic test use and amniocentesis and karyotype. The latter cost was based on a 75% amniocentesis uptake rate, the source of which was not given. The quantity/cost boundary adopted was the hospital. The date of the price data was not stated.

**Statistical analysis of costs**

Standard deviations, correlation coefficient, variance, covariance and means.

**Currency**

UK pounds sterling (€).

**Sensitivity analysis**

A threshold analysis was used to report the results in the 'synthesis of costs and benefits' section. The variable used in this analysis was the cost of the inhibin-A test per woman tested.

**Estimated benefits used in the economic analysis**

Not reported.
Cost results
Not stated.

Synthesis of costs and benefits
The cost per Down’s syndrome pregnancy diagnosed based on estimated gestation age using dates and scan, respectively, was 35,000 and 32,000, for both strategies, when the cost of inhibin-A test was 3.50 and for a given cost of free Beta-hCG of 1.50. A cost above or below the 3.50 threshold for the inhibin-A test would be associated with the intervention having a higher or lower average cost-effectiveness ratio.

Authors’ conclusions
The inhibin-A based four marker test is the most effective method of prenatal screening for Down’s syndrome suitable for routine use. If the extra cost required to carry out the inhibin-A test were less than about 3 per woman screened, the four marker test including inhibin-A would be financially cost-effective.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used.

Validity of estimate of measure of benefit
The study design used in the effectiveness study was appropriate for the study question/hypothesis. The estimated benefits are likely to be internally valid.

Validity of estimate of costs
Adequate details about the costs were not given.

Other issues
Appropriate comparisons were made with other studies. The estimates of screening performance are likely to be generalisable to other countries but will vary to a limited extent in countries with different maternal age distributions from that in Britain. The authors’ conclusions were based on average rather than incremental cost-effectiveness ratios.

Implications of the study
The results of this study are likely to be reliable and are supported by a meta-analysis of all similar studies.

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