Cost-effectiveness of estimating gestational age by ultrasonography in Down syndrome screening

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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 ultrasound estimation of gestational age in maternal serum screening for Down's Syndrome.

Type of intervention
Screening.

Economic study type
Cost-benefit analysis.

Study population
Pregnant women undergoing screening for Down's Syndrome. Maternal ages ranged from less than 15 years to 49 years.

Setting
Not stated but presumably the screening was carried out at ante-natal clinics in the USA.

Dates to which data relate
The clinical effectiveness data were based on a study published in 1997 (see other publications of related interest). The price year was not stated.

Source of effectiveness data
The evidence for clinical effectiveness was based on a retrospective review of screening carried out in the authors’ laboratories (see other publications of related interest).

Link between effectiveness and cost data
The cost data were derived retrospectively from the same sample as that used in the clinical effectiveness study.

Study sample
The sample consisted of 24,313 women at 15.0 to 21.9 weeks gestation. 10,068 women had LMP-based dating and 14,245 women had ultrasound-determined gestational ages. When both ultrasound and LMP data were available, ultrasound dating was preferentially used. Women with large discrepancies between the reported LMP and gestational age estimated by physical examination were likely to have received an ultrasound examination. The LMP group therefore consisted of women whose dating before the test was considered reliable enough for test interpretation. Gestational age and screening results were compared for 24 Down's Syndrome pregnancies in which both ultrasonography and LMP dating were available. The sample appears to have been appropriate to the study question.
No details were provided relating to the methods of sample selection, power calculation for sample size or rates of those refusing to participate or those excluded from the sample. Note: some of this information has been taken from the abstract of the original study (see other publications of related interest).

Study design
Retrospective review of laboratory data. The study appears to have been carried out in a single centre.

Analysis of effectiveness
The study was retrospective in design, and presumably all data were therefore based on treatment completers. The primary health-related outcomes were sensitivity and false-positive rates for Down's Syndrome. Data were not provided to demonstrate the degree of group comparability, and adjustment for confounding variables was not mentioned.

Effectiveness results
Ultrasound dating generally provided higher sensitivities and lower false-positive rates than LMP dating. At advanced maternal age, the sensitivity appeared to be marginally lower with ultrasound dating, but this difference was small. The differences in sensitivities and false-positive rates for the two methods of dating at each maternal age were statistically significant (p<0.05, chi-square test), with the exception of sensitivity at age 39. For ultrasound dating, the sensitivity ranged between 51.8% for maternal age less than 15 years and 99.5% for 49 years, and the false-positive rate ranged from 3.0% to 92.3%. For LMP dating, the sensitivity ranged between 41.9% and 100.0%, and the false-positive rate ranged from 3.4% to 96.6%. Based on the distribution of maternal ages for pregnancies in the USA in 1995, the overall expected performance for ultrasound-based testing corresponded to a 72% sensitivity and 7.1% false-positive rate, whereas for LMP-based referrals, the sensitivity was 67% and the false-positive rates were 8.6%.

Clinical conclusions
When ultrasound dating is available before serum screening, it should be used preferentially to establish the risk of Down's Syndrome.

Modelling
To determine the maternal age-specific sensitivity and false-positive rates for ultrasound- and LMP-based testing, population simulations were carried out using a computer programme (see other publications of related interest).

Methods used to derive estimates of effectiveness
To determine the maternal age-specific sensitivity and false-positive rates for ultrasound- and LMP-based testing, population simulations were carried out using a computer program (see other publications of related interest).

Estimates of effectiveness and key assumptions
A second-trimester risk of 1:270 was used as the cut-off to define a screen-positive result. The second-trimester incidence of Down's Syndrome was based on the regression formula of Cuckle et al (see other publications of related interest), with 23% adjustment for the loss of unaffected pregnancies between the time of screening and full term.

Measure of benefits used in the economic analysis
The following formula was used to derive the per case net benefit (NBi) of maternal screening (see other publications of related interest): NBi = -Pi + 241,174 Si I - 840 Fi (1-I). Pi = the cost of the screening test I; Si = the sensitivity of a screening test; I = the incidence of Down's Syndrome in the second trimester; and Fi = the false-positive rate of a prenatal screening test.
The formula incorporated fees, intrauterine survival rates, and utilisation rates for the various components of screening and follow-up. The uptake rate for amniocentesis was 70% and the survival rate of foetus after amniocentesis was 99.5%. Down’s Syndrome termination rate was 90% and the Down’s Syndrome foetal survival rate was 77%. The estimated benefits cost $504,000 and the cost of triple test was $70. The cost of amniocentesis was $1,200 and the cost of pregnancy termination was $2,000. The cost of second trimester ultrasound was $250 and the cost of recalculating a test result $5. Benefits are expressed in monetary terms. The net benefits for LMP- and ultrasound-based tests were calculated using the separate Down’s Syndrome incidences that corresponded to the mean ages for each group (28.3 and 26.9 years, respectively). The sensitivity rates and false-positive rates used to calculate net benefit were based on revised rates (i.e. after any adjustments to risk because of gross inaccuracies in dating).

**Direct costs**
Fees were derived from a national database of fees for medical services (see other publications of related interest). The average net benefit per case was determined from the 1995 pregnancy population data for the USA, with individual years interpolated from five-year interval data (see other publications of related interest). Sensitivity and false-positive rates were derived by modelling as described above. Per-patient costs of any additional expenses (post-screening ultrasound, repeat testing, and recalculations) incurred in both groups were estimated. It was assumed that the total number of women with a documented recalculation of Down’s Syndrome risk constituted the entire number of women who received ultrasound examination as a result of positive screening tests. A fee of $250 was assumed for each of these ultrasound examinations. A fee of $70 was assumed for the triple-test; a repeat of this was recommended when the error in gestational age was more than 10 days and the initial test had been done before 15 weeks gestation. A non-recovered cost of $5 was also assumed for recalculation after a major revision in the gestational age estimation. Fees for amniocentesis were estimated as $1,200 whether or not a patient had received a previous ultrasound scan. The quantity/cost boundary was that of the health service. Costs and quantities were presented separately for ultrasound examination, repeat testing, recalculation of test results, and additional ultrasound examinations. Discounting and the price date were not mentioned.

**Statistical analysis of costs**
Statistical tests were not reported.

**Indirect Costs**
In the discussion section, the authors stated that the non-medical expenses for families involved in raising an individual with Down’s Syndrome were included in the study.

**Currency**
US dollars ($).

**Sensitivity analysis**
Not reported.

**Estimated benefits used in the economic analysis**
See the synthesis of costs and benefits field below.

**Cost results**
Of the 10,068 LMP-based referrals, 505 women had documented ultrasound examinations that cost $126,250 (505 x $250), or an average of $12.54 for each case. Costs for repeat testing were $19,600 (280 x $70) or $1.95 per case. Costs for recalculation of test results were $960 (192 x $5) or $0.10 per case. Costs for additional ultrasound examinations were $250 (9 x $250) or $0.16 per case, and for repeat testing were $560 (8 x $70) or $0.04 per case. The net additional costs associated with the LMP-based referrals were therefore $14.39 plus the $31.60 in lost net
benefits, for a total of $45.99.

Synthesis of costs and benefits
The range of net benefits for ultrasound dating were from $4.27 at a maternal age of less than 15 years to $33,538.74 at 49 years. The corresponding values for LMP dating were -$17.90 and $33,671.31. The difference in net benefit ranged from $22.18 for less than 15 years and -$132.57 for 49 years. Without ultrasound dating, testing had a negative net benefit for women up to the age of 26. However, a positive net benefit was shown for all ages when ultrasound dating was available. The difference in net benefit between the dating methods was not constant across ages; the difference in net benefit was greatest at age 39 ($69.57). For maternal ages of 45 years or more, the net benefit appeared to be greater using LMP dating. Using the maternal age distribution for 1995, the average net benefit for the triple test using ultrasound dating was $185.99 and for LMP dating was $152.44. The average loss in net benefit when ultrasound dating was not used was therefore $33.54. The average loss in net benefit due to the absence of ultrasound dating was estimated as $31.60.

Authors' conclusions
Routine first-trimester ultrasound examination can be justified for women with a known LMP if the cost of the ultrasound examination is less than $46.

CRD COMMENTARY - Selection of comparators
The use of LMP dating as a comparator for ultrasound dating of gestational age seems to be appropriate. Problems with the use of LMP dating are outlined in the introductory section of the paper.

Validity of estimate of measure of benefit
The clinical effectiveness data were based on a retrospective review of laboratory data. Potential problems associated with the use of retrospective studies include incomplete and poor quality data and bias in interpretation. However, a large sample of women was available for analysis. The benefit results were derived from a model which produced extensive age-specific outcomes and determined net benefits in monetary terms. Appropriate parameters were used in its construction.

Validity of estimate of costs
Fees were derived from a national database of fees for medical services, presumably a reliable source. Discounting was not mentioned. Costs and quantities were presented separately for ultrasound examination, repeat testing, recalculation of test results, and additional ultrasound examinations. The price year used was unclear. The study perspective was mainly that of the health service.

Other issues
It is difficult to comment on the generalisability of this study as few details were available describing the characteristics of the study sample. Comparisons with similar studies were described.

Implications of the study
Authors' statement: Health policy makers need to recognise the total societal aspects of medical services such as screening, for which the benefits can be far broader than the provision of clinical care.

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Other publications of related interest


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