Choroid plexus cysts in the mid-trimester fetus: practical application suggests superiority of an individualized risk method of counselling for trisomy 18


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
This study considered an individualised risk method and an average risk method of counselling for trisomy 18 in pregnant women, where at least one choroid plexus cyst (CPC) was detected in the second trimester foetus.

The individualised risks were calculated by multiplying the prior risk of trisomy 18 (determined by maternal age or multiple-marker screening results) by the likelihood ratio of 9 (established by Gupta et al, see Other Publications of Related Interest) if the CPC was isolated (no other abnormalities were found on ultrasound). If the CPC was associated with other foetal ultrasound anomalies (complicated CPC or cCPC), the patient was advised of a high risk of aneuploidy and offered amniocentesis.

Using an average risk method, the patient was advised of a 1 in 150 risk of aneuploidy if one or more CPC were found without other ultrasound anomalies.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised pregnant women who had been referred to a prenatal diagnostic centre with a CPC detected in the second trimester.

Setting
The setting was tertiary care. The geographical setting of this study appears to have been San Diego (CA), USA.

Dates to which data relate
The effectiveness and resource use data related to August 1995 to September 2001. The price year was not reported.

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

Link between effectiveness and cost data
The resource use data for the intervention group were collected from the same patient sample that provided the effectiveness data. The resource use of the comparator group was estimated.
Study sample
All patients referred to the unit where the study was taking place, during the study period, were eligible for inclusion in the study. Patients who were lost to follow-up (n=11), where there was disagreement over the presence of a CPC (n=2), where the CPC was discovered after the results of the karyotype (n=5), and where medical records could not be traced (n=5), were excluded from the study. The final cohort included 395 patients, of which 341 had an isolated CPC and 54 were found to have other foetal ultrasound abnormalities (cCPCs). This study did not include a control group, as the results from the intervention group were compared with a hypothetical group. No sample size or power calculations were reported.

Study design
This study was a single-centre retrospective cohort study that followed pregnant women to the end of their pregnancy. The retrospective nature of the study means that patients who were lost to follow-up were excluded at the start.

Analysis of effectiveness
The measures of effectiveness were the incidence of trisomy 18 and the sensitivity and specificity of amniocentesis screening, based on the two approaches. All patients initially included in the study appear to have been accounted for in the analysis. The analysis of benefits was confined to the population of isolated CPCs. The authors noted that the benefit of amniocentesis in the setting of cCPCs was generally accepted.

Effectiveness results
The incidence of trisomy 18 was 17% (9 of 54) in the population of cCPCs and 0.6% (2 of 341) in the population of isolated CPCs.

The sensitivity of the average risk method was 100% and the specificity was 0.6%. If all patients with an individualised risk of 1 in 200 or greater were offered amniocentesis, the sensitivity of screening remained at 100% but the specificity increased to 1.6%. If the level of individualised risk where amniocentesis was offered was reduced to 1 in 100, the sensitivity of screening remained at 100% but the specificity increased to 3.0%. If the individualised risk threshold level was lowered to 1 in 50, the sensitivity would still be 100% but the specificity would have risen to 5.6%.

Clinical conclusions
The authors concluded that the use of an individualised method of counselling for risk of trisomy 18 increased the specificity of trisomy 18 detection, without reducing its sensitivity.

Measure of benefits used in the economic analysis
No summary outcome measure was used in the economic analysis. The study was, in effect, a cost-consequences analysis.

Direct costs
The perspective adopted was not stated. The only cost included was the cost of amniocentesis. The authors assumed that all women offered this test would take it up. The unit costs and the quantities were reported separately. The source of the cost data and the price year used were not reported. Discounting was not used, but this was appropriate since the time scale was less than one year.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
No indirect costs were included in the study.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analysis was undertaken.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The total cost of amniocentesis, if average risks were used, was $409,200.

The total cost of an individualised risk assessment depended on the level of risk accepted. Using a level of risk of 1 in 200, the total cost was $153,600 if all women with a 1 in 200 risk took up amniocentesis. The total cost was $79,200 at a level of risk of 1 in 100 and $43,200 at a level of risk of 1 in 50.

The average cost per case of trisomy 18 detected was $204,600 with the average risk method and $76,800 with an individualised risk method (at a level of risk of 1 in 200).

**Synthesis of costs and benefits**
Not relevant since the study was, in effect, a cost-consequences analysis.

**Authors' conclusions**
The use of an individualised method of counselling for risk of trisomy 18 resulted in net savings in a referred population of prenatally detected choroids plexus cysts (CPCs), without lowering the sensitivity of detection.

**CRD COMMENTARY - Selection of comparators**
The authors did not provide a clear justification for their choice of the comparator. They noted, according to their experience, that many practitioners continue to counsel for isolated CPC based on an average risk of trisomy 18. You should consider how their comparator relates to usual practice in your setting prior to applying the results of this study.

**Validity of estimate of measure of effectiveness**
The effectiveness of screening was derived from a retrospective cohort study with a hypothetical comparator. This had the potential to introduce bias into the study. A retrospective cohort study with a control group would have been more appropriate to answer the study question. The paper included insufficient details of the method used to assess the individualised risks (maternal age and results of serum screening were not reported). The method used to evaluate the specificity of the two methods was unclear. The authors did not consider whether their study sample was representative of the study population. The population characteristics were not reported. Despite the limitations of the study design, the analysis of the resultant data appears to have been credible.

**Validity of estimate of measure of benefit**
The authors did not derive a summary measure of health benefit for use in the economic analysis. The study was, in effect, a cost-consequences analysis.
Validity of estimate of costs
The paper was lacking in detail about the estimation of the costs. The source of the cost data was not reported. This makes it very difficult to assess whether the study may be applicable to other settings. No price year was reported, which means that future reflation exercises are not possible. No statistical or sensitivity analyses were undertaken on any of the cost data or related assumptions. This means that the degree of uncertainty around the results was not assessed, thus the generalisability of the results is limited. The only cost covered in this analysis was the cost of undertaking amniocentesis. The economic perspective of the study was not reported. The potential cost of complications and other services that may be required as a result of the screening programme were not considered.

Other issues
The authors discussed their findings in relation to other related studies and discussed the differences. They did not consider how their findings might be generalisable to other settings. The paper is limited by the incomplete presentation of economic data. The authors' conclusions reflected the data presented. However, they recommended that individualised risks be used, without a clear assessment of whether their results could be generalised. Sensitivity analyses, to account for variability in the cost or effectiveness data, were not performed. Consequently, caution should be exercised if extrapolating the study results to different contexts.

Implications of the study
The authors recommended that individualised risks should be used to decide whether to offer amniocentesis where a choroid plexus cyst, but no other ultrasound abnormalities, is found. They suggested that further large series are needed to confirm their results.

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Other publications of related interest

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