Comparison of different strategies in prenatal screening for Down's syndrome: cost effectiveness analysis of computer simulation
Gekas J, Gagne G, Bujold E, Douillard D, Forest JC, Reinharz D, Rousseau F

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.

CRD summary
The objective was to assess and compare the cost-effectiveness of different strategies for prenatal screening for Down's syndrome. The authors concluded that contingent screening, with a first trimester cut-off value for high risk of one in nine, was the preferred option. Overall the methodology was appropriate, and both the methods and results were, in general, well reported. The authors’ conclusions appear to be appropriate for the scope of their analysis.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to assess and compare the cost-effectiveness of different strategies for prenatal screening for Down's syndrome and to determine the most useful risk cut-off values for screening.

Interventions
The screening strategies, which were compared with amniocentesis in women 35 years old or older, were: the integrated test; sequential screening; contingent screening; and triple test. The sequential and contingent screenings consisted of a sequence of tests with many possible cut-off values for the risk of the foetus having Down's syndrome. The risk cut-off values for the first trimester tests were: one in six, one in nine, one in 30, one in 58, one in 114, one in 175, one in 237, and one in 307. In total, 19 screening strategies were compared.

Location/setting
Canada/out-patient secondary care.

Methods
Analytical approach:
A decision tree model was used to simulate the 19 screening options. The time horizon was the end of pregnancy. The authors reported that the perspectives were that of the Canadian Ministry of Health and the Public Medical Assurance.

Effectiveness data:
The effectiveness and clinical data were derived from a number of published studies. Many of the model parameters were populated with data from the Serum Urine and Ultrasound Screening Study (SURUSS, Wald, et al. 2003, see 'Other Publications of Related Interest' below for bibliographic details). The main effectiveness parameter was the screening test performance, which was the marker values in pregnancies affected by Down’s syndrome and in unaffected pregnancies. This information was derived from the SURUSS.

Monetary benefit and utility valuations:
None.

Measure of benefit:
The measure of benefit was the number of cases of Down’s syndrome detected.

Cost data:
The costs comprised those of screening and medical services relating to the following outcomes: birth, spontaneous
miscarriage, elective abortion after positive results, and pregnancy loss after a diagnostic test. These direct costs included those of screening; consulting with a genetic counsellor; chorionic villous sampling; amniocentesis; and termination of pregnancy. All the costs included those of necessary support services such as administration and cleaning. The costs for laboratory and imaging tests were derived from technical units for Quebec, whilst other costs were derived from government databases. The price year was 2007 and all costs were reported in Canadian dollars (CAD).

Analysis of uncertainty:
A series of univariate sensitivity analyses were performed to assess how robust the model results were to variations in the model parameters based on information from other sources. In addition, 95% confidence intervals for the incremental cost-effectiveness ratios were generated using 100 replications of the population.

Results
The number of cases of Down's syndrome detected per 100,000 pregnancies was: 56.12 with amniocentesis; 101.40 to 112.72 with contingent screening, depending on the cut-off value; 100.88 to 112.46 with sequential screening, depending on the cut-off value; 87.16 with integrated test; and 87.48 with triple test.

The total cost per 100,000 pregnancies was: CAD 4.1549 million with amniocentesis; CAD 2.7529 million to CAD 4.1999 million with contingent screening; CAD 3.6265 to CAD 5.0960 with sequential screening; CAD 3.3944 with integrated test; and CAD 3.8324 with triple test.

The costs and benefits were combined in an incremental cost-effectiveness ratio (ICER) or the additional cost per case of Down's syndrome detected. Compared with amniocentesis, most of the screening interventions were dominant, which means they were more effective and less costly. The exceptions were contingent screening at a cut-off value of one in 307, which had an ICER of CAD 795 and sequential screening with cut-offs of one in 175 (ICER CAD 5,096), one in 237 (ICER CAD 11,096), and one in 307 (ICER CAD 16,704).

These results were robust in the sensitivity analysis.

Authors' conclusions
The authors concluded that contingent screening, with a first trimester cut-off value for high risk of one in nine, was the preferred option for prenatal screening for Down's syndrome.

CRD commentary
Interventions:
The interventions were reported clearly and in detail. An explicit justification was given for using the comparator, which was that amniocentesis for women over 35 years old was the standard in North America and Europe.

Effectiveness/benefits:
The effectiveness and clinical data were derived from published studies. The authors did not report how these studies were sought nor the methods used to select them. This means it is not possible to determine if all the relevant information was included. The authors reported that much of the information was derived from the SURUSS. The references for this study were adequately reported, but the details of the study, such as the sample size and method of randomisation, were not reported. The main effectiveness and clinical parameters were reported, as were the values used in the model, and their sources.

Costs:
The perspective was explicitly reported and all those cost categories and costs, relevant to the public health care system, appear to have been included. The sources from which these costs were derived were adequately reported. The price year and currency used were reported.

Analysis and results:
A decision tree model was used to synthesise all the evidence and full details of this model and a diagram were given.

The impact of uncertainty on the model's results was considered through one-way sensitivity analyses, but probabilistic...
sensitivity analysis would have been a more thorough and complete way of capturing the overall model uncertainty. The authors reported the methods used to calculate 95% confidence intervals, but these results were not reported. The authors adequately highlighted the limitations of their study, such as that their results were based on mathematical modelling and not on prospective observational data.

Concluding remarks:
Overall the methodology was appropriate, and both the methods and results were, in general, well reported. The authors’ conclusions appear to be appropriate for the scope of the analysis.

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