Cost-effectiveness and accuracy of prenatal Down syndrome screening strategies: should the combined test continue to be widely used?

Gekas J, Durand A, Bujold E, Vallee M, Forest JC, Rousseau F, Reinharz D

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
This study examined the cost-effectiveness of various strategies of prenatal screening for Down's syndrome, including quadruple, combined, integrated, and serum integrated tests, and stepwise or contingent sequential screening. The authors concluded that their findings did not support the use of the combined test, but contingent screening was cost-effective. The cost-effectiveness methods were valid, but more extensive reporting of the data sources would have helped in judging the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of various strategies for prenatal screening for Down's syndrome, including quadruple, combined, integrated, and serum integrated tests, and stepwise or contingent sequential screening.

Interventions
The eight screening strategies were quadruple, triple, combined, integrated, serum integrated, sequential, contingent, and age.

Quadruple was a second-trimester test based on the measurement of alpha-fetoprotein, unconjugated oestriol, free beta-human chorionic gonadotrophin (β-hCG), and inhibin-A, as well as maternal age.

Triple was the same as quadruple, but without inhibin-A.

Combined was a first-trimester measurement of nuchal translucency, free β-hCG, and pregnancy-associated plasma protein A (PAPP-A), with maternal age.

Integrated was the combination of measurements performed at different times of pregnancy into single test; nuchal translucency and PAPP-A in the first trimester and quadruple test in the second trimester.

Sequential was the triple test in the first trimester, with a diagnostic test (chorionic villous sampling) if the results were positive and a quadruple test in the second-trimester if they were negative.

Contingent was the same as sequential, but women at very low risk did not receive the second screening.

Age was amniocentesis offered to all women aged 35 years or more.

Location/setting
Canada/primary care.

Methods
Analytical approach:
The analysis was based on a published decision-tree model, with a hypothetical cohort of 110,948 pregnant women. A short-term horizon of the birth was considered. The authors stated that the perspective of the public health sector was adopted.

Effectiveness data:
Relevant sources of evidence were selected. The accuracy of the screening tests was the key input and was from a
published clinical trial, called the Serum, Urine, and Ultrasound Screening Study (SURUSS). The uptake of the diagnostic tests after positive screening was from a Canadian source.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The number of Down's syndrome births detected was the benefit measure. Other relevant endpoints, such as the false-positive rate, procedure-related euploid miscarriages, Down's syndrome live births, and unnecessary terminations, were reported.

Cost data:
The economic analysis included the costs of the screening tests and the medical costs of birth, spontaneous miscarriage, elective abortion, or procedure-related euploid miscarriage. The costs were from government databases and provincial technical units. The resource quantities depended on the test strategies. All costs were in Canadian dollars (CAD) and the price year was 2007.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on selected inputs (the rate of consent to participate in prenatal screening, the rates of foetal loss from chorionic villous sampling and from amniocentesis, and the proportion of couples with a confirmed Down's syndrome foetus who chose pregnancy termination). Alternative estimates were based on authors’ opinions. The sensitivity and false-positive rates of the screening strategies were varied over the ranges observed in the SURUSS trial. Bootstrap methods were used to generate 95% confidence intervals around the model outcomes.

Results
In the whole cohort, the total costs (in millions) were CAD 2.8579 with contingent, CAD 2.7906 with serum integrated, CAD 3.7440 with sequential, CAD 3.2610 with integrated, CAD 5.3476 (CAD 4.1613 alternative data) with combined, CAD 4.413 with quadruple, CAD 3.8324 with triple, and CAD 4.1549 with age. The number of Down's syndrome cases detected was 106.51 with contingent, 88.87 with serum integrated, 106.32 with sequential, 90.35 with integrated, 113.25 (114.00 alternative data) with combined, 88.19 with quadruple, 87.48 with triple, and 56.12 with age.

The most cost-effective strategy was contingent screening, with an average cost per Down's syndrome case detected of CAD 26,833 and an incremental cost per Down's syndrome case detected of CAD 3,815, over serum integrated screening, which was the second most cost-effective strategy. Screening based on age alone was the least cost-effective option. These findings were robust in the sensitivity analyses.

Most of the other outcomes were similar for the contingent and sequential screening strategies. Among those strategies with a low rate of procedure-related miscarriage, contingent screening reassured 78.4% of patients in the first trimester and 79% of women did not have a second-trimester test. The combined test identified the most Down's syndrome pregnancies in the first trimester, but had the highest number of procedure-related euploid miscarriages and of unnecessary terminations.

Authors' conclusions
The authors concluded that their findings did not support the combined test, but contingent screening was cost-effective.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the available screening strategies were considered. A description of each option was given.

Effectiveness/benefits:
The studies used for the clinical inputs were presumably those known to the authors, as a systematic search of the literature was not reported. The test accuracy was the key model parameter and was from a large clinical trial. These are
generally considered to be valid clinical sources, but no details of the trial were given, which makes it difficult to fully judge the quality of the data. Most of the data were from a previous model and were not described in this report. The benefit measure was specific to the interventions studied and might not be comparable with the benefits of other health care interventions.

Costs:
The cost categories and the data sources appear to have been consistent with the perspective adopted as government price lists were used. The unit costs of each screening test and procedure were reported, together with the resource use for each strategy. The cost estimates were specific to the study setting and the impact of variations in these estimates was not tested.

Analysis and results:
The costs and benefits of each strategy were clearly reported. Average cost-effectiveness ratios were presented for all strategies, while the incremental cost per unit of benefit was reported only for contingent screening. The authors stated that the health care heterogeneity across countries might affect the external validity of their results. A deterministic approach was used to investigate the uncertainty and it focused on selected inputs. The calculation of confidence intervals showed the variability in the results.

Concluding remarks:
The cost-effectiveness methods were valid, but more extensive reporting of the data sources would have helped in judging the authors’ conclusions.

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