

Cost utility of prenatal diagnosis and the risk-based threshold

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Summary

Background Prenatal testing guidelines recommend offering amniocentesis or chorionic villus sampling to women aged 35 years or older, or who have been found by screening to be at a similarly high risk of giving birth to an infant with Down's syndrome or another chromosomal abnormality. This threshold was chosen, in part, because 35 was the approximate age at which amniocentesis was cost beneficial when testing guidelines were developed in the USA in the 1970s. We aimed to assess the economic validity of thresholds based on age or risk for offering invasive prenatal diagnosis.

Methods We did a cost-utility analysis of chorionic villus sampling and amniocentesis versus no invasive testing using data from randomised trials, case registries, and a utility assessment of 534 diverse pregnant women aged 16–47 years.

Findings In the USA, compared with no diagnostic testing, amniocentesis costs less than US\$15 000 per quality-adjusted life year gained for women of all ages and risk levels. The results do not depend on maternal age or risk of Down's syndrome-affected birth. The cost-utility ratio for any individual woman depends on her preferences for reassurance about the chromosomal status of her fetus, and, to a lesser extent, for miscarriage.

Interpretation Prenatal diagnostic testing can be cost effective at any age or risk level. Current guidelines should be changed to offer testing to all pregnant women, not just those whose risk of carrying an affected fetus exceeds a specified threshold.

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Introduction

Current prenatal diagnosis guidelines throughout much of the world recommend offering invasive testing (chorionic villus sampling or amniocentesis) to women who are at a high risk of having a fetus that is chromosomally abnormal.^{1,2} The risk of a chromosomal disorder increases with advancing maternal age, and, when antenatal testing guidelines for invasive testing were established in the USA in the late 1970s, a consensus emerged that amniocentesis should be reserved for women aged 35 years or older.³ This threshold was chosen because at that age the procedure-related miscarriage risk was approximately equal to the chance that a child will be born with Down's syndrome⁴ and the costs of offering amniocentesis would be offset by the savings associated with preventing the birth of an infant affected by Down's syndrome.^{5–7}

The discovery of serum and ultrasonographic markers that can be used to refine risk estimates for Down's syndrome has further entrenched these risk-based guidelines for offering invasive testing. Pregnant women of all ages are now screened routinely for Down's syndrome, and are referred for invasive testing if their midtrimester Down's syndrome risk is higher than a given threshold, typically that of the average 35 to 37 year old.⁸ However, offering diagnostic testing only to women whose risk is above the threshold introduces several related difficulties. First, because women at low risk are not offered the option of diagnostic testing, use of a risk threshold does not allow them to decide for themselves whether their risk of carrying a chromosomally abnormal fetus is sufficiently high to make incurring the miscarriage risk of a diagnostic procedure reasonable. Second, setting the threshold at the approximate age at which the procedure-related miscarriage and Down's syndrome risks are equal implicitly assumes that women are equally concerned about these two outcomes.⁹ We have shown in our previous work that this assumption is not true.^{10,11} Moreover, the current approach ignores preferences for several other outcomes of testing decisions, including obtaining information about the chromosomal status of the fetus during pregnancy.¹² Finally, restricting use of prenatal diagnosis to populations in which its use is cost beneficial imposes an economic criterion that conflicts with accepted standards of cost-effectiveness.¹³

Many economic analyses of prenatal diagnostic testing have been published in the past two decades. When prenatal testing thresholds have been discussed, however, the focus has remained on determining the most appropriate threshold, rather than assessing whether a population-based threshold should, in fact, be used.¹⁴ And when the possibility of preference-based guidelines has been raised, it has been addressed hypothetically, without analysis of the effect of pregnant women's measured preferences on the cost-effectiveness of testing.^{15,16}

In this study, we investigated the merit of the risk-based thresholds that underlie current prenatal diagnostic testing

guidelines by use of cost-utility analysis, a standard economic technique that compares healthcare costs with benefit gained (in terms of Quality-Adjusted Life Years).¹³ We included a comprehensive set of outcomes associated with the procedures (including miscarriage and future births after pregnancy losses, and the presence or absence of information about the fetus' chromosomal status); and we used preference weights (utilities) from a large racially or ethnically and socioeconomically diverse sample of pregnant women of all ages as the basis for quality adjustments. We then investigated the effect of allowing all women—not just those meeting a specific risk criterion—to make informed decisions about whether to undergo prenatal diagnostic testing for chromosomal disorders.

Methods

Decision model

We built a decision model to assess the cost utility of chorionic villus sampling and amniocentesis compared

with no diagnostic testing for pregnant women of all ages and risk levels. The model addresses the decision to undergo diagnostic testing based on age-adjusted risk or revised risk estimates after screening. Figure 1 presents a simplified version of the decision model, based in part on our previous work.¹² The model includes several possible outcomes of diagnostic testing decisions, including birth of a baby that does not have a chromosomal disorder, birth of a baby affected by a chromosomal disorder, miscarriage, elective abortion after positive test results, and whether a future birth occurs after a pregnancy loss. Also accounted for in the model, but not presented in the figure, are test performance characteristics for chorionic villus sampling and amniocentesis, birth with a limb abnormality after chorionic villus sampling, and timing of miscarriage depending on the test undergone.

The model follows outcomes starting with the tenth week of pregnancy, before any diagnostic testing has been done. It then follows the pregnancy, birth, and remainder of the woman's life expectancy. The bottom branch in figure 1 models the group who does not undergo chorionic villus sampling or amniocentesis. These women have a baseline miscarriage risk that varies depending on whether the fetus is affected by a trisomy.^{17–21} If a woman has a pregnancy loss, we explicitly incorporate the possibility that she might give birth in the future.

If a woman chooses to undergo amniocentesis, she is at risk of a miscarriage before she has the test, and either before or after the test results are given. If the test is positive, a woman may choose to terminate the pregnancy. Although infrequent, false positive and false negative test results were included in the calculations.^{22,23} The chorionic villus sampling group is similar to the amniocentesis group, except that costs, miscarriage risks, test performance, and the probability of future births after miscarriages or elective abortions differ. In addition, we include the possibility that tissue sampling or culture for chorionic villus sampling might be unsuccessful—thus needing follow-up amniocentesis.

Data used in analysis

In the analysis, we relied on randomised controlled trials to provide data where possible. Otherwise, we considered case series, case-control studies, and observational studies (see table 1 for data used and ratings of data quality). We included trisomies 13, 18, and 21 to incorporate the most prevalent trisomies that are identified by prenatal diagnosis. We incorporated risks, life expectancy, and costs of each trisomy separately. When we estimated sensitivity ranges on estimates, we used 95% CIs based on point estimates from randomised trials or case series. Where trials were combined, we used a broad range consisting of the upper and lower 95% CIs from the contributing studies.

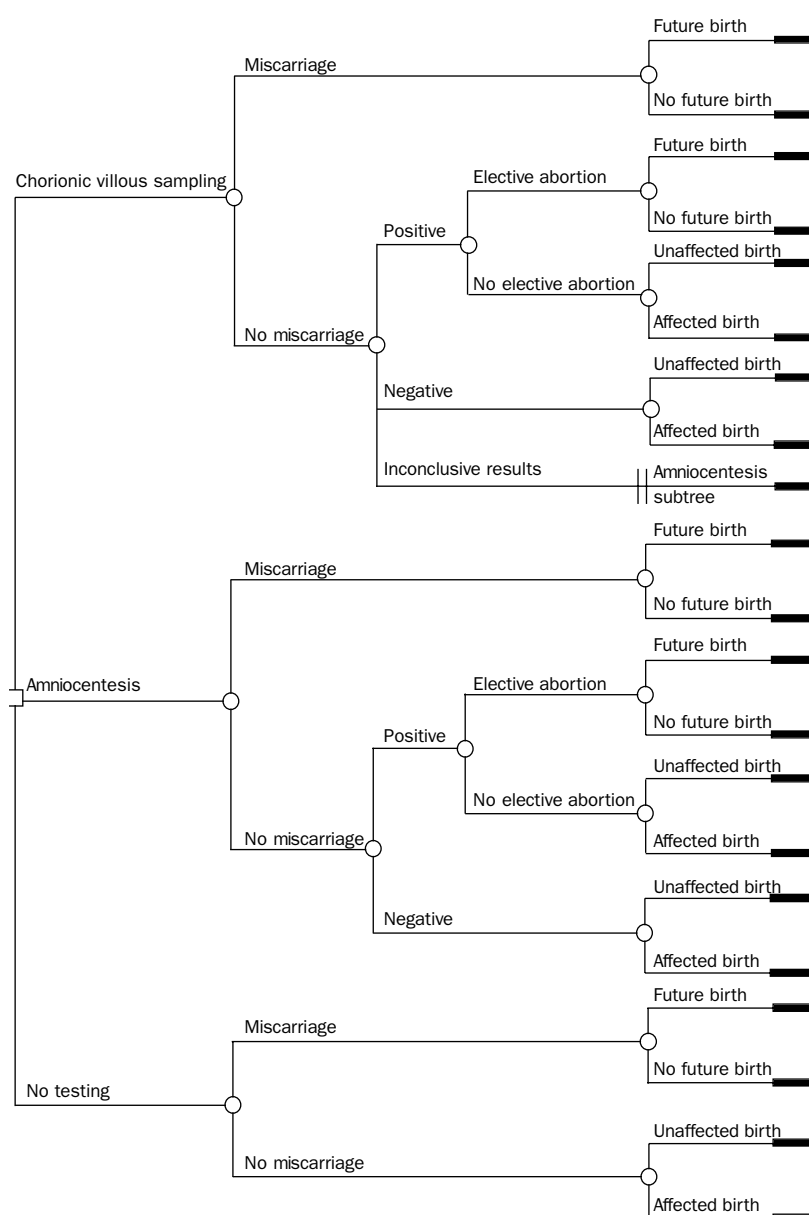


Figure 1: Schematic representation of decision model

Not shown in this simplified depiction, but included in our model, is the possibility that miscarriage occurs before testing or after results and that false positive and false negative test results can occur after amniocentesis or chorionic villus sampling.

	Base case (% range)*	Data quality†	Source
Trisomy risk at week 10	0.58 (0.19–22)	II-2	19,20
Miscarriage risk			
Excess risk of amniocentesis compared with no testing	0.75 (0.27–1.47)	I	24 adjusted with 25
Excess risk of CVS compared with amniocentesis	1.4 (0.5–4.44)	I	22,23 adjusted with 19,25
Test performance			
Sensitivity			
Amniocentesis	99.32 (98.6–100)	I	Combination of results from 23,24
CVS	98.47 (97.5–100)	I	Combination of results from 23,24
Specificity			
Amniocentesis	99.86 (99.8–100)	I	Combination of results from 23,24
CVS	99.83 (99.5–100)	I	Combination of results from 23,24
Probability of a future birth			
After amniocentesis and miscarriage	40.9 (20–60)	II-2	11,26
After CVS and miscarriage	50.0 (30–70)	II-2	11,26
After amniocentesis and elective abortion	32.8 (20–60)	II-2	11,27
After CVS and elective abortion	27.9 (15–55)	II-2	11,27
Other probabilities			
Diagnostic uncertainty with CVS, requiring amniocentesis	6.48 (2.95–8.6)	I	22,23,28
Elective abortion after abnormal results	92.9 (60.0–95)	II-2	29 weighted by 17
Limb abnormality after CVS	0.0058 (0.0–0.096)	II-2	30
Utilities‡			
Testing, normal results, unaffected birth	0.923 (0.62–1)	II-2	..
No test, unaffected birth	0.918 (0.63–1)	II-2	..
Testing, miscarriage, future unaffected birth	0.870 (0.51–1)	II-2	..
Testing, miscarriage, no future birth	0.700 (0.18–1)	II-2	..
Testing, elective abortion, future unaffected birth	0.836 (0.40–1)	II-2	..
Testing, elective abortion, no future birth	0.692 (0.13–1)	II-2	..
Testing, normal results, affected by limb abnormality	0.900 (0.41–1)	II-2	..
Trisomy (Down's syndrome)	0.672 (0.13–1)	II-2	10
Costs§			
CVS	\$1220 (500–2000)	II-2	31,32
Amniocentesis	\$1120 (500–2000)	II-2	31,32
Miscarriage	\$760 (400–900)	II-2	31–33
Elective abortion after CVS	\$600 (350–1200)	II-2	31–33
Elective abortion after amniocentesis	\$1060 (530–1245)	II-2	31–33
Prenatal care	\$620 (120–860)	II-2	32
Delivery	\$3940 (2100–6200)	II-2	32,34 and OSHPD database
Autosomal trisomies (weight-averaged cost of trisomy 13, 18, and 21 incremental to unaffected baby)¶	\$228 400 (150 000–300 000)	II-2	35

CVS=chorionic villus sampling. I=randomised controlled trial. II-2=cohort or case-control trial. OSHPD=California Office of Statewide Health Planning and Development. *Used in one-way sensitivity analyses. Based on 95% CI where possible, or structured as broadly as possible to create a conservative analysis. †Ratings based on US Preventive Services Task Force guidelines.³⁶ ‡Time tradeoff scores on a scale in which 1=perfect health for mother and baby equals and 0=death. For women older than 45 years, we adjust for declining utility of current health.³⁷ §All costs in 2003 US\$ and discounted to the present at a 3% discount rate. ¶Included only in sensitivity analyses.

Table 1: Data used in base-case analysis

Probabilities

Trisomy probability—The age-specific probability that a fetus at 10 weeks' gestation is affected by trisomy 13, 18, or 21 came from an investigation of trisomies in more than 4000 chorionic villus sampling procedures.^{19,20}

Miscarriage risk—Estimation of procedure-related miscarriage risk was complicated because the chance of miscarriage depends on the chromosomal status and gestational age of the fetus. In addition, some fetuses electively aborted after testing would have spontaneously aborted before delivery. We calculated the procedure-related risks as follows. The amniocentesis miscarriage risk (0.75% relative to no test) was based on a randomised study of 4606 women.²⁴ We calculated the difference in miscarriage rates in the two groups. To this value, we added the number of elective abortions that would have been miscarriages had elective abortion not taken place.²⁵ We used the same technique to calculate the chorionic villus sampling miscarriage risk. The miscarriage risk of chorionic villus sampling was based on a randomised study of 2787 women (1.4% relative to amniocentesis).²³ Because there is disagreement about procedure-related miscarriage risks, as well as belief that such risks may depend on the facility where the

procedures are done, we varied these estimates substantially. These ranges in estimates covered results from other studies and results with different calculation techniques.^{22,28}

Test performance—Although both amniocentesis and chorionic villus sampling are excellent diagnostic tests, neither is perfectly accurate. We calculated sensitivity and specificity by combining results from the two largest randomised trials that compared these procedures.^{22,23} We weighted each trial by the number of patients tested, and accounted for cytogenetic and sex typing errors. We assessed these estimates thoroughly in sensitivity analyses. Included in the ranges were figures presented in the Eucromic report³⁸ on the accuracy of 62 865 chorionic villus sampling procedures.

Some chorionic villus sampling samples are inconclusive because of maternal cell contamination, insufficient tissue acquisition, or culture failure. We chose one randomised study²² as a baseline estimate of inconclusive test results (6.48%) and varied this estimate on the basis of ranges of results from other trials and reports.^{23,28,38,39} In our analysis, we assumed that all inconclusive chorionic villus sampling results lead to amniocentesis.

Future births—How women feel about miscarriage depends on whether they can conceive again.¹¹ The probability of a future birth after a pregnancy loss came from two studies that tracked reproductive outcomes after miscarriage or elective abortion subsequent to prenatal diagnosis.^{26,27}

Other probabilities—We used a study²⁹ of pregnancy termination in 26 950 women who underwent amniocentesis to estimate the chance that a woman will choose elective abortion after a positive test (92·9%). To account for the possibility that chorionic villus sampling slightly increases the risk of transverse limb-reduction defects (by 0·0058%), we used data from a registry that followed the results of 80 000 chorionic villus sampling procedures and 1 million livebirths.³⁰

Preferences for outcomes

Utilities quantify preferences for health states on a scale from 0 to 1.¹³ In this analysis, 0=maternal and fetal death, and 1=perfect health. Our data came from a time-tradeoff utility assessment of 534 English-speaking, Spanish-speaking, or Chinese-speaking pregnant women, aged 16–47 years, from a broad ethnic and socio-economic mix.¹⁰ The time tradeoff approach quantifies preferences by assessing how much time a person is willing to give up to avoid a less-than-ideal outcome.⁴⁰ The assessment procedure involves asking each woman to choose between living her full life expectancy with a less desirable outcome (eg, a child with Down's syndrome) and living a shorter time with an ideal outcome (ie, perfect knowledge of an unaffected fetus without invasive testing, followed by the birth of a healthy child). The time tradeoff utility is defined as the number of years with the ideal outcome divided by the number of years with the less desirable outcome, at the point of indifference. For example, a woman who is indifferent about living for 30 years with a healthy child or 40 years with a child with Down's syndrome has a time tradeoff utility for having a child with Down's syndrome of 0·75 (30 ÷ 40). Time tradeoff utilities were elicited for the eight outcomes included in our decision model. Each outcome description included the type of testing offered, the results of the testing, and the future status of the fetus. For example, amniocentesis, normal results, unaffected birth refers to a scenario in which a woman undergoes

	Quality-adjusted life years*	Lifetime cost	Incremental cost utility†
20 years			
CVS	24·13	\$54 180	Dominated‡
Amniocentesis	24·16	\$54 080	\$14 200
No testing	24·08	\$52 940	
35 years			
CVS	20·35	\$61 590	Dominated‡
Amniocentesis	20·39	\$61 490	\$12 600
No testing	20·30	\$60 360	
44 years			
CVS	17·03	\$59 020	Dominated‡
Amniocentesis	17·08	\$59 020	\$11 300
No testing	16·98	\$57 890	

CVS=chorionic villus sampling. *Life years are life expectancy at ages 20, 35, 44 years, adjusted by the mean utilities associated with that diagnostic test choice (including no testing). Life years and costs are discounted at a rate of 3% per year. Costs are in 2003 US\$. Because of rounding, cost-effectiveness ratios cannot be precisely calculated from costs and life years presented on this table. †Includes all costs of testing, prenatal care, delivery, pregnancy termination, miscarriage, and future healthcare costs of pregnant women. ‡CVS is more costly and less effective than amniocentesis.

Table 2: Quality-adjusted life years, cost, and incremental cost-utility ratios by age

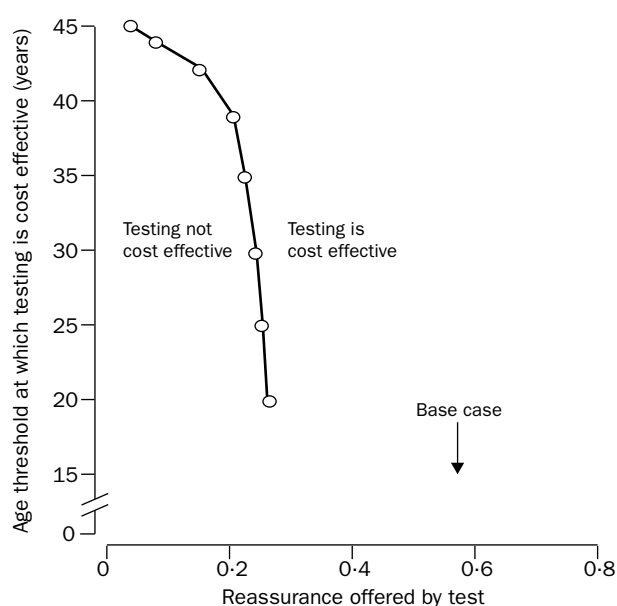


Figure 2: Sensitivity analysis on reassurance offered by test

Results are most sensitive to differences in utilities of two health outcomes: when a woman receives normal test results and gives birth to a chromosomally normal child; and when testing is not done and she gives birth to a chromosomally normal child. The difference in utilities for these two outcomes is the reassurance offered by the test (x axis). Line is point at which testing is cost effective (defined as $\leq \\$50\,000$ per QALY gained).

amniocentesis, receives normal results, does not have a miscarriage during the pregnancy, and then gives birth to an unaffected infant. (Outcome descriptions are available from the authors.)

Costs

We generally used published cost data when such data were available and of high quality. Medical costs were calculated by estimating resource use and applying regional unit costs to these estimates.⁴¹ We used Medicare national limitations³¹ for laboratory costs and the Medicare National Allowable Allowance from the Resource-Based Relative Value Scale³² for physician fees. For inpatient costs, we converted mean hospital charges to costs using a cost-to-charge ratio from the California Office of Statewide Hospital Planning and Discharge database.

The cost of chorionic villus sampling (US\$1220) exceeded that of amniocentesis (\$1120) because of slightly higher physician and ultrasound fees. In calculating the cost of delivery, we estimated that about 25% of deliveries are caesarean sections.³⁴ Furthermore, we incorporated all discounted future health-care costs for the pregnant woman (\$49 110, \$56 620, \$54 120 for a woman aged 20 years, 35 years, and 44 years, respectively).⁴² Omitting the future health-care costs in sensitivity analysis had no effect on the outcome of the analysis.

	Baseline	Threshold value†
Diagnostic testing, miscarriage, future unaffected birth	0·87	<0·72
Diagnostic testing, miscarriage, no future birth	0·70	<0·60
No diagnostic testing, miscarriage, no future birth	0·70	>0·87

*For women aged 35 years. In the base case, amniocentesis costs \$12 600 per QALY gained. †Value that results in an amniocentesis cost-effectiveness ratio that exceeds \$50 000 per QALY gained.

Table 3: One-way sensitivity analyses on selected utilities*

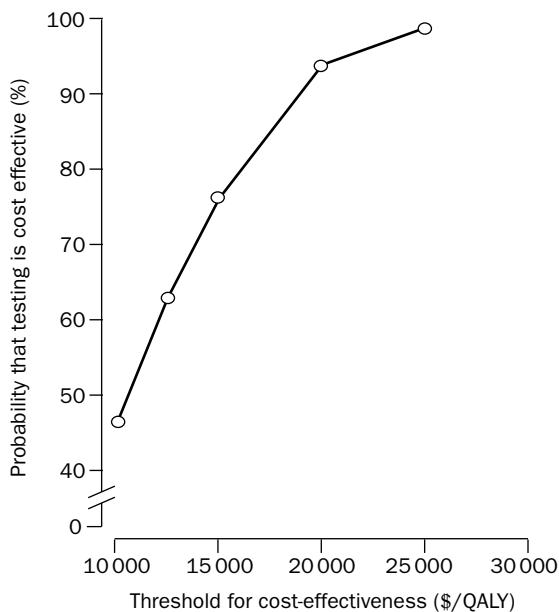


Figure 3: **Probabilistic (Monte Carlo) sensitivity analysis with 50 000 simulations**

Analysis in which all model variables except patient utilities were varied concurrently.

In addition to providing information about fetal chromosomal status to the pregnant woman, prenatal testing avoids subsequent costs associated with raising a child affected by Down's syndrome or another trisomy. Whether the costs associated with Down's syndrome should be included in this type of analysis is controversial.^{13,43} To construct a conservative analysis, we did not include the costs of trisomies averted in the initial base case. However, in sensitivity analysis, we did include the costs of autosomal trisomies (13, 18, 21). We used an incremental lifetime cost of \$228 400 per child with a trisomy, calculated by weight averaging the cost of each trisomy by its prevalence.³⁵ Inclusion of the cost of trisomies had no significant effect on the analysis.

Analyses

We did a baseline analysis from the societal perspective, by use of relevant costs and quality-of-life outcomes associated with testing decisions (including decisions to forego testing). We did one-way, multi-way, and probabilistic (ie, Monte Carlo) sensitivity analyses on all model variables, from the ranges in table 1. In one-way sensitivity analyses, we assumed all other variables were fixed. In multi-way sensitivity analyses, we varied two to eight related variables concurrently, and created relevant clinical scenarios. We reported individual variables and combinations of variables that brought the cost-effectiveness ratio within about 30% of \$50 000 per QALY gained, a frequently used threshold for cost-effectiveness.⁴⁴ Costs were expressed in 2003 US\$. The time frame of the analysis was the pregnant woman's remaining life expectancy beginning in her 10th week of pregnancy. The analysis was done in SMLTREE 2.99. All costs and life years were discounted at a yearly rate of 3%.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Table 2 provides results of the base-case cost-utility analyses for women aged 20, 35, and 44 years. Although we did the analysis for various ages and risk levels, we present these three ages to show the effects of age (or trisomy risk) on the results.

Foregoing diagnostic testing serves as our reference case. At age 35 years, amniocentesis costs about \$1130 more than does no diagnostic testing, but offers an additional 0.09 QALY's, resulting in an incremental cost-utility ratio of about \$12 600 per QALY gained. Because it costs more than amniocentesis but is less effective, chorionic villus sampling is dominated in the base case. As shown in table 2, the cost utility of amniocentesis remains lower than \$15 000 per QALY irrespective of maternal age. Furthermore, these results do not change with wide variations in any of the probability estimates. In short, the cost-utility ratio of prenatal diagnostic testing is low (less than \$15 000 per QALY gained, where less than \$50 000 per QALY gained is within the range of generally accepted health care interventions that are done routinely⁴⁴), does not materially depend on age, and is robust to assumptions about the probability of outcomes.

We did a separate analysis that included the savings associated with the incremental costs of trisomies averted. Inclusion of these costs had no effect on the analysis, decreasing cost utility to \$4600 per QALY gained at age 35 years (\$12 900 per QALY gained at age 20 years). We also found that discount rates did not materially change the results of the analysis. At age 20 years and a discount rate of 8%, cost utility remained lower than \$30 000 per QALY gained. Although our results did not depend on age, the probability of various events, discount rates, or whether trisomy costs were included, the analysis was sensitive to small changes in the difference in women's utilities for the two most commonly experienced outcomes in the model: undergoing diagnostic testing, obtaining normal test results, and giving birth to a chromosomally normal child; and not undergoing testing and then giving birth to a normal child. Because the only distinction between these two outcomes is that the woman knows the fetus has tested negative for chromosomal abnormalities, the difference between these two utilities reflects the value of reassurance offered by the test.

Figure 2 shows how the results change with the value of reassurance as quantified by this difference in utilities: as the reassurance offered by the test increases, the age at which testing is cost effective declines. Figure 2 also shows that amniocentesis is cost effective for all women, irrespective of age, if the decrease in quality of life from not having chromosomal information is greater than about 0.25%. Compared with other negative health outcomes, 0.25% is small. For example, 0.25% approximates the decrease in quality of life from the burden of taking aspirin every day.⁴⁵ The average decrease in quality of life from not having chromosomal information reported in our study was about 0.6%.

Table 3 shows three other utilities to which the results are sensitive. When the utility of testing, miscarriage, and future unaffected birth is less than 0.72 (baseline value: 0.87), amniocentesis costs more than \$50 000 per QALY gained. Similarly, when the utility of testing, miscarriage, and no future birth is less than 0.60 (baseline value: 0.70), amniocentesis costs more than \$50 000 per QALY gained. Furthermore, when the utility of no testing followed by a miscarriage without a future birth is greater than 0.87 (baseline value: 0.70), amniocentesis again costs more than \$50 000 per QALY gained. As before, trisomy costs were not included.

Finally, figure 3 shows the results of a probabilistic sensitivity analysis in which we ran 50 000 simulations, concurrently varying all model variables with the exception of patient utilities. We did not vary utilities in this particular analysis because differences among individuals are patient specific rather than due to measurement error or uncertainty. As the figure shows, the model was insensitive to simultaneous changes in all of the non-utility variables. In more than 99.98% of the 50 000 simulations, the cost utility of testing was less than \$30 000 per QALY gained.

Discussion

We have shown that prenatal diagnostic testing for chromosomal disorders is cost effective irrespective of maternal age or risk of carrying an affected fetus. By use of accepted cost-utility methods, we found no economic evidence to support the existing guidelines that recommend offering prenatal diagnostic testing only to women aged 35 years or older, or to women with a similar risk as determined by maternal serum screening, ultrasonography, or both. In fact, we found no age threshold below which prenatal diagnosis would be cost ineffective (greater than \$50 000 per quality-adjusted life year gained).

Although the results did not depend on age or risk, they were very sensitive to the preferences that individual pregnant women have for the outcomes of testing. In particular, desire for the reassurance offered by the test (as measured by the decrease in quality of life from not having chromosomal information) had an important effect on our results. The more reassurance women desire, the more cost effective is the testing. Moreover, utilities for miscarriage and for future birth also affected the outcome of the analysis.

Together, these findings call into question the use of risk thresholds for offering chorionic villus sampling and amniocentesis. Because preferences for prenatal testing outcomes are personal and vary substantially,^{12,13} our findings suggest that prenatal diagnosis should be offered to pregnant women irrespective of age or risk (because such testing can be cost effective, depending on the woman's preferences), and that special attention should be paid to the preferences of the individual on offering such testing, including the desired level of reassurance the patient needs (because individual preferences can greatly affect the cost utility of testing). Instead of focusing on thresholds for offering or denying testing on the basis of age or risk alone, guidelines should emphasise ways to support informed choice by women of all ages and risk levels. We recognise that implementation of such a policy change could be challenging. If substantially more women choose to be tested, the number of cytogenetic labs, counsellors, and doctors to do the procedures might increase. Furthermore, additional training and new communication tools would be needed for antenatal providers to help assess women's preferences in addition to presenting risk information. Nonetheless, our analyses suggest that such resource use is appropriate.

Our study has several limitations. First, because results from randomised studies were not available for every variable in the model, we used non-randomised studies as the basis for some of our estimates. The data we used, however, were the best available and include large case series with thousands of patients. Sensitivity and Monte Carlo analyses showed, moreover, that wide variations in these variables had little effect. Second, we focused the analysis only on autosomal trisomies, the most prevalent

serious chromosomal disorders that lead to viable fetuses. Cost, quality-of-life, and epidemiological data are also strongest in the area of autosomal trisomies. However, including other disorders in the analysis would only enhance the cost utility of diagnostic testing. Finally, we did not independently assess the cost utility of maternal serum or ultrasonographic screening for Down's syndrome and other trisomies. Instead, we focused on the core assumption underlying current recommendations for invasive diagnostic testing: that the age or risk cutoff for referral for chorionic villous sampling or amniocentesis should be a risk at least as high as that of an unscreened 35-year-old woman. Although guidelines for use of maternal serum and ultrasonographic screening also need to be explored, the cost-effectiveness of diagnostic procedures depends entirely on the 35-year-old-or-similar risk threshold, leading to our focus.

In summary, we found that cost-utility analysis does not support the current practice of reserving chorionic villus sampling and amniocentesis for women who are 35 or older, or who are at similarly high risk of carrying a fetus affected by a chromosomal abnormality. Instead, prenatal diagnostic testing should be offered to pregnant women irrespective of maternal age or risk, and guidelines should emphasise the important role of individual preference when making decisions about prenatal diagnostic testing.

Contributors

R Harris was responsible for the design and implementation of the cost-utility analysis and for writing the initial draft of this report. A E Washington participated in study design, interpretation of results, and manuscript preparation. R F Nease participated in the design, implementation, and interpretation of the analysis and in report writing. M Kuppermann was the primary investigator for this project and had overall responsibility for the conception and execution of the project, working closely with R Harris in all aspects of study design and implementations, and report writing.

Conflict of interest statement

None declared.

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