

Routine Prenatal Screening for Congenital Heart Disease: What Can Be Expected? A Decision-Analytic Approach

ABSTRACT

Objectives. This study assessed the potential impact of fetal ultrasound screening on the number of newborns affected by cardiac anomalies.

Methods. A decision model was developed that included the prevalence and history of congenital heart disease, characteristics of ultrasound, risk of abortion, and attitude toward pregnancy termination. Probabilities were obtained with a literature survey; sensitivity analysis showed their influence on expected outcomes.

Results. Presently, screening programs may prevent the birth of approximately 1300 severely affected newborns per million second-trimester pregnancies. However, over 2000 terminations of pregnancy would be required, 750 of which would have ended in intrauterine death or spontaneous abortion. Further, 9900 false-positive screening results would occur, requiring referral. Only the sensitivity of routine screening and attitude toward termination of pregnancy appeared to influence the yield substantially.

Conclusions. The impact of routine screening for congenital heart disease appeared relatively small. Further data may be required to fully assess the utility of prenatal screening. (*Am J Public Health.* 1997;87:962-967)

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Introduction

Over the last decade many reports have appeared on the possibilities of ultrasound for prenatal detection of congenital heart disease, but few authors have tried to assess the actual yield of a screening program for cardiac anomalies.¹⁻¹⁵ It is important to distinguish between a limited screening procedure offered routinely to all pregnant women (population approach) and extensive fetal echocardiography offered to those at (high) risk for fetal congenital heart disease.

In the population approach, all pregnant women undergo routine ultrasound examination at a certain optimal gestational age. When a congenital anomaly is suspected, referral to establish a diagnosis and appropriate obstetric policy follows. The screening procedure currently advocated for routine evaluation of the fetal heart is the four-chamber view at 16 to 24 weeks of pregnancy.^{3,6}

The high-risk approach is generally accepted and offers extensive fetal echocardiography to selected women, in particular to those women with a history of congenital heart disease in their offspring or those who appear during routine screening to be carrying an affected fetus.¹⁶ Anomalies encountered in the high-risk group tend to be more serious and complex. In addition to the four-chamber view, the cardiac connections and functional status are evaluated.¹⁶ Obviously, this can only be accomplished by skilled experts during a lengthy and detailed examination.

To justify routine prenatal screening in low-risk pregnancies with subsequent extensive ultrasound examination in case

of suspected fetal pathology, an assessment of the efficiency of such a program is needed. Presently, however, a favorable effect of routine fetal ultrasound including a four-chamber view evaluation is assumed. Routine fetal ultrasound is now offered to the majority of pregnant women in several countries, including the Netherlands. To our knowledge, this policy has not been preceded by an appropriate evaluation. Medical decision analysis offers a possibility for integrating and analyzing the influence of the efficacy of screening, the risks for the affected fetus, and societal or parental attitudes on the expected distribution of outcomes of pregnancy in a low-risk population.

We set out to assess whether the advantages of prenatal detection of cardiac anomalies by means of ultrasound examination are sufficiently clear to merit screening of pregnant women at low risk for congenital heart disease in their offspring.

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Methods

Structure of the Model

The present report proceeds from an inventory of data available in the literature. These data have been introduced into a decision analysis model centered on the problem of whether to offer routine fetal echocardiography to pregnant women at low risk. Decision Maker software (New England Medical Center, Boston, Mass, 1988) was used to structure the model. The options and chances future parents, clinicians, and policymakers face at 16 to 24 weeks' gestational age are conveyed (Figure 1). The high-risk approach as a separate option was not included in the model, as its merits have been established.^{6,8,17-20} In addition, as spontaneous abortion or intrauterine death prior to a prenatal diagnostic procedure is not amenable to intervention, this possibility was not evaluated. The probability of an affected fetus (with minor or major congenital heart disease) was considered in the model at the first chance node. The subsequent chance node in the model represents routine fetal echocardiography. Given a malformation in the fetus, the chance of a positive test result is the sensitivity. Similarly, the chance of a negative test given the absence of malformations is the specificity.

The subsequent branch of the model represents referral on suspicion of an anomaly at initial screening. Extensive fetal echocardiography is offered to those screened and found to have a suspected fetal anomaly. Also, those presenting pregnancy pathology—for example, growth discrepancy, lack of fetal movements, or abnormal fetal heart rate—are referred. For the model we assumed that extensive fetal echocardiography would in general reveal previous false-positive diagnostic errors (100% specificity). This appears to be a reasonable simplification of the model, since further diagnostic tests or termination of pregnancy are not offered unless a (serious) fetal anomaly is indeed suspected. Nonadoption of screening implies that extended ultrasound is available only in the event of clinically suspected fetal or pregnancy pathology. Similar to the test characteristics of routine screening, the test characteristics of extensive fetal echocardiography have been applied in the model.

In case an anomaly is confirmed at extensive fetal ultrasound examination, chorion villus sampling, amniocentesis, or cordocentesis is offered. These techniques

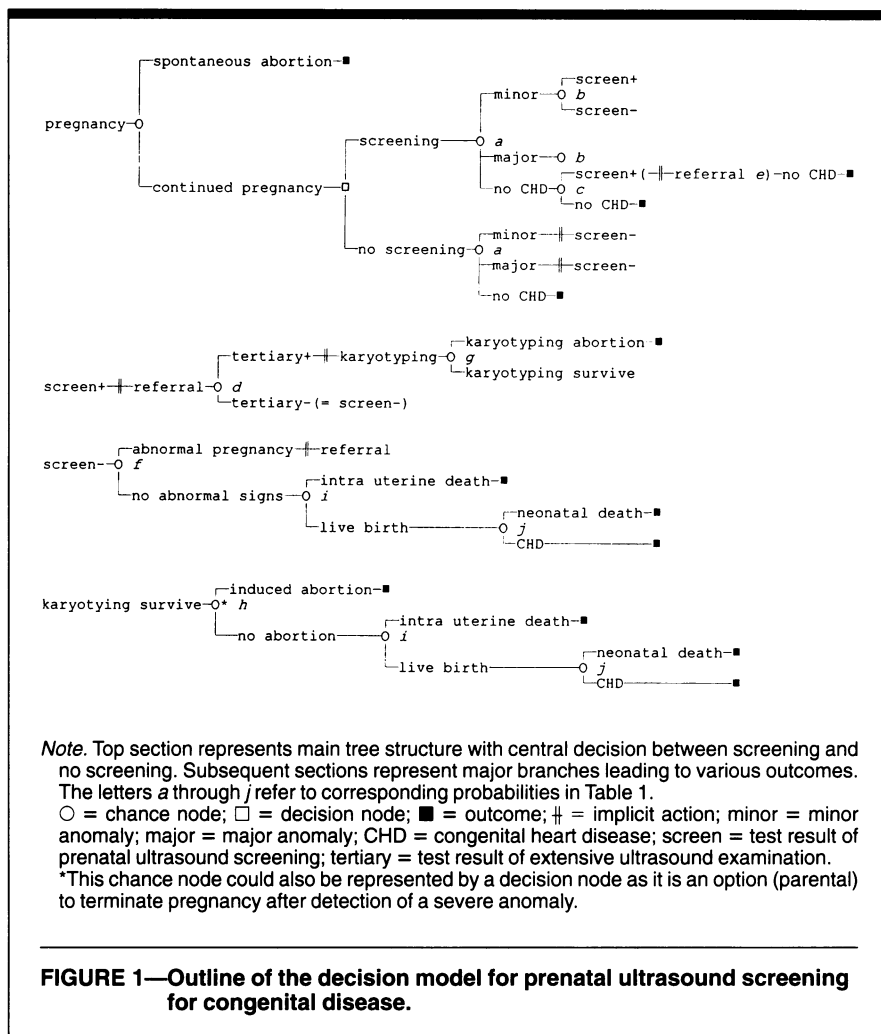


FIGURE 1—Outline of the decision model for prenatal ultrasound screening for congenital disease.

have a low risk of induced abortion. This risk is represented by the corresponding chance node in the model.

The next step is the decision parents face when confronted with the diagnosis and prognosis of their fetus. They may choose to terminate the pregnancy or carry to term. Obviously, an unaffected fetus or a fetus with minor anomalies is likely to be carried to term. In case the gestation of a fetus with congenital heart disease is continued, two outcomes are possible: intrauterine death or a live infant with a cardiac anomaly. As a result of the anomaly the infant may die postnatally. The risk of a fatal outcome is again represented by a chance node. The situation is essentially similar if parents informed of the presence of a fetal anomaly decide not to terminate the pregnancy, if an anomaly is not detected, or if screening is not offered.

Assignment of Probabilities

All variables used in the model are summarized in Table 1. A number of

problems in the assignment of probabilities need to be discussed. An estimate of the chance of a fetus with congenital heart disease is preferably based on the prevalence of cardiac anomalies at 16 to 24 weeks' gestation. However, while the prevalence of congenital heart disease at birth is well documented, reliable estimates at about 20 weeks' gestational age are sparse. We assumed that newborns with a birth prevalence of cardiac anomalies of approximately 0.008²¹ originated from a larger cohort of fetuses of which a proportion aborted spontaneously or ended in premature death. In addition, it should be noted that only about half of the cardiac anomalies found in neonates are major anomalies.²² Assuming that approximately 37% of the major anomalies end in premature death,^{19,20} the number affected at 20 weeks' gestation was calculated at 10.3 per 1000 (0.004 + 0.004*1/1-0.37).

The test characteristics of routine and extensive ultrasound examination used in the analysis are based on a literature survey. Some studies reported

TABLE 1—Estimates of the Various Probabilities Applied in the Decision Model on Routine Fetal Ultrasound Examination for Congenital Heart Disease (CHD)

	Point Estimate	Lower Value	Upper Value	Major Anomalies	Minor Anomalies
Prevalence ^{21,22}	0.008	0.003	0.012	0.004	0.004
a. Prenatal prevalence ^a	0.0103	0.0063	0.004
b. Sensitivity routine screening ¹⁻¹⁵	0.07	0.07	0.50	0.50	(0.20-0.80)
c. Specificity routine screening ¹⁻¹⁵	0.99	0.99	1.0	...	(0.01-0.20)
d. Sensitivity extensive ultrasound ^{6,8,17-19}	0.95	0.927	0.974
e. Specificity extensive ultrasound ^{b 6,8,17-19}	0.99	0.987	0.993	1.00	1.00
f. Probability abnormal pregnancy given CHD	0.01	0.01	(0-0.03)
g. Probability karyotyping induced abortion ²³	0.01	(0-0.03)
h. Probability termination of pregnancy given CHD ^{8,19,20}	0.678	0.571	0.773	0.68	(0-1.0)
i. Probability intra uterine death given CHD ^{19,20}	0.370	0.194	0.576	0.37	(0.20-0.60)
j. Probability neonatal death given CHD ^{19,20}	0.588	0.329	0.816	0.59	0.1

Note. In the analysis a distinction is made between major and minor anomalies. The plausible range used in sensitivity analysis is given in parentheses. Major and minor are categories of congenital malformation according to which sensitivity and clinical course is varied in the model. Ellipsis points indicate estimates of variables or ranges of variables not examined in the current analysis. The letters *a* through *j* refer to corresponding probabilities in Figure 1.

^aExpected prevalence at 20 weeks' gestation calculated; varies according to probability of intrauterine death given CHD.

^bIn the model a specificity of extensive fetal echocardiography of 100% is applied.

on a high-risk population and a more extensive screening procedure, whereas others reported on a low-risk population and a simple screening procedure performed once during pregnancy. This resulted in a wide range of published results.¹⁻¹⁵ To account for this variability we assumed the test characteristics, especially the sensitivity, to vary according to case severity. Accordingly, the upper range of sensitivity reported (around 50%) was taken to apply to serious cases, whereas the lower range of literature estimates (below 10%) was taken to apply to minor anomalies. The specificity of routine screening is reported to be very high (99%) and has a narrow range. The sensitivity of extensive fetal ultrasound evaluation appears to be much better and has been reported at around 95% with a narrow range.^{6,8,17-20} Also, a near 100% specificity of extensive fetal ultrasound examination has been reported.^{6,8,17-20} Detailed data on extensive fetal echocardiography enabled us to calculate the test characteristics with the specific indication of suspected fetal (cardiac) pathology.^{8,19,20} The likelihood of abortion as a complication of fetal karyotyping is low (less than 1%).²³ Data on the probability of pregnancy pathology in relation to congenital heart disease could not be found. A panel of obstetricians at Rotterdam University Hospital estimated the probability at less than 1%. In case a malformation is detected parents have to decide whether to terminate the pregnancy. Specific literature on this subject is

scarce. Pryde et al. evaluated several factors influencing parental decisions regarding pregnancy outcome of congenitally malformed offspring.²⁴ The prognosis appeared to be of major importance; two out of three couples opted to terminate pregnancy if a major anomaly was detected. Termination was never opted for in case of minor anomalies. Similar results have been reported in relation to extensive fetal echocardiography.^{8,19,20,24}

With regard to the prognosis of affected fetuses, a distinction between serious and mild cases was also made. Cases detected prenatally are likely to be a subsample with severe anomalies. Accordingly, the outcomes of pregnancy reported in case-series on cases detected prenatally are taken to apply to serious cases. Intrauterine death occurred in 37% of such cases and infant death in 59%.^{19,20} On the other hand, children with congenital heart disease born alive may represent a subsample with relatively mild anomalies. Live-born children with congenital heart disease have a mortality of less than 10%. This is the estimate of survival used in the model in case of minor cardiac malformations. In addition, we assumed that the majority of minor anomalies do not cause hemodynamic problems prenatally. Accordingly, the fetuses survive to term. Finally, a sensitivity analysis was conducted over plausible ranges of the probabilities (as presented in the right-hand side of Table 1) to assess the influence of variability in the estimates on the outcome of the model.

Results

The impact of routine screening, in numbers per million second-trimester pregnancies, is given in Table 2. With an assumed low sensitivity of 50% for major anomalies, it is estimated that the number of children born with severe congenital heart disease decreases by a third. A similar effect on the number of cases of intrauterine death and neonatal death is observed. Some of the intrauterine deaths and neonatal deaths that would otherwise have occurred are avoided if pregnancy is terminated in cases detected prenatally.

The impact of routine screening on the number of children born with minor congenital heart disease is negligible. The number of terminations of pregnancy would, however, increase 50-fold. Also, approximately 9900 false-positive screening tests would result. Moreover, screening would lead to a loss of 32 fetuses, 28 with major anomalies and 4 with only minor anomalies, owing to karyotyping. As we presumed a specificity of extensive fetal echocardiography of 100%, karyotyping is not offered to unaffected fetuses. An increase in sensitivity (to 80% and 20% for major and minor anomalies, respectively) will reduce the number of cases with an unfavorable outcome (from 525 fewer to 841 fewer for births of infants with serious anomalies and from 757 fewer to 1211 fewer for neonatal deaths). For minor anomalies the change is negligible. Obviously, more pregnancies will have to be terminated to achieve this

reduction (from 2005 to 3208). In addition, as a result of a higher sensitivity, fetal karyotyping is performed more often, causing an additional loss of 23 (affected) fetuses (increasing the number lost from 32 to 55). Also, a sizable number of the cases that otherwise would have resulted in intrauterine death or spontaneous abortion are now terminated (from 752 fewer to 1205 fewer). If sensitivity decreases, only a marginal effect remains. However, an identical number of women would have to be referred and go through an emotionally difficult period owing to a false-positive screening test.

Parental inclination toward termination of pregnancy in case of severe malformation appears to have an effect that is numerically comparable to increased sensitivity of routine ultrasound. Obviously, with an increased proportion of the parents opting for termination of pregnancy in case of a major anomaly, fewer affected neonates are born. If all pregnancies are carried to term very little effect remains.

Figure 2 shows the results of a two-way sensitivity analysis of the two major determinants of the impact of screening. The effect of simultaneously varying estimates of the sensitivity of routine fetal ultrasound and estimates of the proportion of parents opting for termination of pregnancy, both in case of a severely affected fetus (i.e., cases resulting in neonatal survival with severe congenital heart disease or cases ending in neonatal death), is demonstrated. The number of newborns with serious anomalies prevented increases with increasing sensitivity and with an increasing probability of termination of pregnancy. Sensitivity and probability of termination show a combined (multiplicative) effect.

Variation in the probability of abnormal development of pregnancy or pregnancy pathology in affected fetuses does not appear to have any significant impact. Neither does variation in the probability of intrauterine death. We assumed the birth prevalence of congenital heart disease to remain stable. Accordingly, an increased probability of premature death implies that a larger number of pregnancies are terminated that would otherwise result in intrauterine death. Also, a larger number of affected fetuses would be lost owing to karyotyping. (Additional details and results are obtainable from the authors.)

TABLE 2—Estimated Pregnancy Outcomes of 1 Million Second-Trimester Pregnancies (Fetuses of 16 to 24 Weeks' Gestational Age)

Outcome	No Screening	Screening	Difference	% Change ^a
Major congenital heart disease	1 629	1 104	-525	-32
Minor congenital heart disease	3 600	3 597	-3	<-0.1
Neonatal death	2 745	1 988	-757	-28
Termination of pregnancy	41	2 046	2 005	49 ^b
Karyotyping-induced abortion	1	33	32	32 ^b
Intrauterine death	2 334	1 582	-752	-32
No congenital heart disease (false-positive)	0	9 897	9897	∞ ^b
No congenital heart disease	989 651	979 754	-9897	-1

^aPercentage change relative to no screening.

^bAs the percentage change would exceed 100, a multiplier is presented.

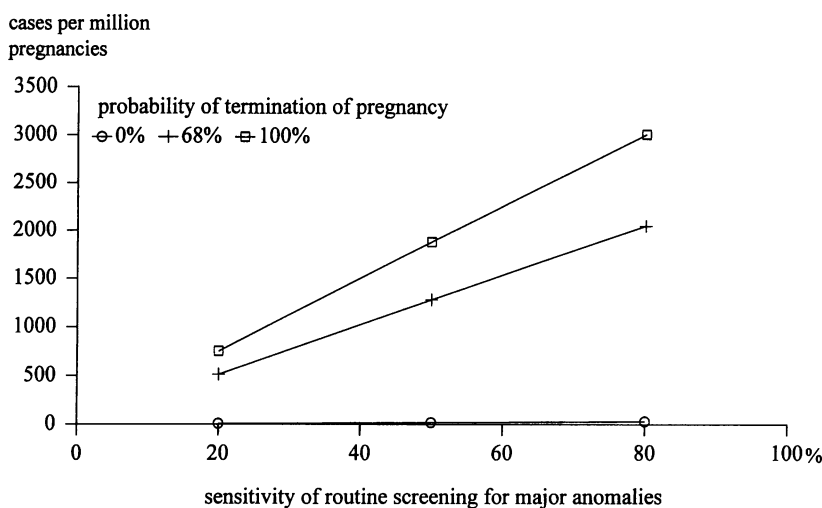


FIGURE 2—Results of the two-way sensitivity analysis for the sensitivity of routine screening for major anomalies and the probability of termination of pregnancy (impact of screening vs no screening on number of newborns with serious anomalies prevented).

Discussion

We have shown that routine fetal ultrasound screening does not meet the generally held expectations. The fundamental idea of screening is that parents, neonates, and society in general may benefit from effective screening. One of the initial assumptions in the model was that approximately half of all severe anomalies would be detected prenatally. On prenatal detection of an anomaly, the obstetric policy may be adapted. If, for instance, a case of Fallot's tetralogy with severe pulmonary stenosis were detected prenatally, soon after birth the diminished pulmonary flow could result in a life-threatening situation. Birth should prefer-

ably take place in a setting able to provide pediatric intensive care. With prior knowledge, timing, mode, and location of delivery can be optimized to improve chances of neonatal survival. In cases with a (near) fatal prognosis, termination of pregnancy presently is the main alternative.^{7,8,19,20,24-26}

According to the model, the birth of approximately 30% of neonates with serious congenital heart disease may be prevented. However, as a consequence 49 times as many pregnancies have to be terminated, of which again 30% would have ended in spontaneous abortion. Also, some affected fetuses will be lost in any case owing to karyotyping. The hypothetical yield of routine fetal ultrasound

appears to be relatively small. Moreover, in view of recently reported realistic estimates of the sensitivity of routine fetal ultrasound, only a few cases with an unfavorable outcome of pregnancy may actually be prevented.^{27,28} Even if optimal estimates of sensitivity apply, the impact of prenatal screening for congenital heart disease on the health of neonates in general appears limited. This conclusion is in agreement with that of Nelson et al., who reported that a large proportion of fetal anomalies are not likely to be diagnosed, especially in a nonreferral setting.²⁹ The nature of the anomalies encountered prenatally predicts, to a large extent, the possibilities for early detection. Moreover, routine fetal ultrasound has additional disadvantages. Even a false-positive rate of only 1% results in a large number of parents' being told that their future baby may have congenital heart disease. If the specificity in reality is 1% lower, doubling the false-positive rate, twice as many such cases occur. Apart from the anxiety caused by such news we must consider the implications for the referral institutions. All of these women will subsequently be referred for extensive ultrasound evaluation. The investments in personnel, appliances, and clinics required are sizable and revenues are small.

A second variable that was shown to affect the attainable yield was the opinion future parents (or society in general) hold on termination of pregnancy. The proportion of pregnancies terminated on account of serious congenital heart disease will depend strongly on such an opinion or preference. In other words, the impact of screening will vary with local legal and ethical standards and attitudes.

We are aware of the fact that the basis for some of the other variables examined was uncertain. However, the impact of variability of these estimates on the expected distribution of outcomes of pregnancy in a low-risk population appeared to be limited. Moreover, the test characteristics of extensive structural ultrasound can already be considered more or less optimal, as are the complication rates of fetal karyotyping. Also, the actual prevalence, the natural history, and factors affecting the natural history of congenital malformations are hardly accessible to intervention. If they were accessible, this would imply possibilities for primary prevention.

Finally, an additional remark should be made regarding the specificity of extensive fetal echocardiography. The

specificity applied in the model was presumed to be 100%. Therefore, far-reaching consequences of false-positive routine screening tests are absent in the model and in the results presented. This may not be quite correct. Recently, cases have been described of fetuses with apparently severe congenital heart disease that proved to have only mild to moderate anomalies postnatally.³⁰ A false-positive rate of extensive fetal echocardiography of 1% (specificity 99%) would result in approximately 100 such cases (1% of 9897) in the hypothetical cohort. Future parents erroneously presented with a serious prognosis who opted to terminate pregnancy would lose a normal fetus.

Overall, the yield of prenatal screening for congenital heart disease by means of the fetal four-chamber view, expressed as the prevention of the birth of a critically ill neonate, appears to be numerically small. With substantial effort the efficacy of routine screening may be improved. However, the results would still be modest. Moreover, the final decision parents make once a serious fetal anomaly is detected is culturally, socially, and economically determined. Evidently, a generally applicable protocol for termination of pregnancy is unrealistic.

The significance and valuation of the cases detected, cases not detected, and false-positive test results and their subsequent outcomes have not been assessed in the present analysis. Such an assessment may be attempted by estimating the psychological relief or burden perceived by the parents. Additionally, the costs of screening and postnatal costs could be weighed against the effects. Heckerling and Verp²³ and Pauker and Pauker^{31,32} assigned specific values or utilities to the various outcomes of pregnancy in a prenatal Down's syndrome screening program. Subsequently the utility of screening was estimated. Ekwo et al. also reported on the outcome of pregnancy with regard to congenital anomalies and the perceived consequences or burden.³³ The parents' opinion on the outcomes of pregnancy could be expressed on a preference scale. At present, reliable data on parental attitudes toward congenital heart disease are lacking, as are data on the costs of congenital heart disease. Yet parental assessment of the various outcomes may have a substantial impact on the appreciation and efficiency of a prenatal screening program for congenital anomalies. After all, the parents decide whether or not to have prenatal screening

and how to respond to the outcome of the test.

In conclusion, routine fetal ultrasound screening for congenital heart disease does not seem warranted at present. Public health, in particular neonatal health, is not likely to improve if prenatal screening is offered in low-risk pregnancies. The public expenditures involved could more effectively be spent otherwise. □

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