

## Fetal Anomaly Screening for Detection of Congenital Heart Defects

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### Abstract

Congenital heart defects remain the most common congenital malformation in live births and are the leading cause of infant mortality in the developed world. Major developments in the management over the last decade have led to significant improvements in survival of infants with congenital heart defects. Early diagnosis and timely appropriate management of critical and serious CHDs is essential to improve outcome. Fetal anomaly screening is being used to detect the critical and significant congenital heart defects prenatally between 18+0 weeks and 20+6 weeks of pregnancy. This helps professional and parents in critical decision making regarding the pregnancy, planning for delivery and preparing the parents for the anticipated problems. Prenatal diagnosis of critical congenital heart conditions has shown to improve the outcome in infants with critical congenital heart defects.

**Keywords:** Congenital heart defect; Infant; Fetal anomaly

### Background

Congenital heart defect (CHD) is defined as defect in the heart and major blood vessels, including structural, chromosomal, genetic, biochemical defects and malformations. CHD is the most common congenital malformation in live births with an incidence of around 1% in general population. The incidence of critical CHD (needing intervention or operation within 1 month after birth) is around 2 per 1000. CHDs remain a leading cause of infant mortality accounting for up to 40% of all deaths from congenital defects. Up to 7.5% of the infant mortality in the developed world is reported from CHDs.

Major developments in diagnosis and management over the last decade have led to dramatic improvements in survival with more than 85% of children diagnosed with CHD now surviving into adulthood. Early diagnosis and timely appropriate management of critical and serious CHDs is essential to improve outcome.

Current screening tests are fetal anomaly screening (FAS) and routine examination of newborn. Pulse oximetry screening has been shown an effective screening method to detect critical CHDs and fulfils the criteria for universal screening. It's being recommended by most professional bodies involved in the care of children with CHDs and currently being adopted by many countries across the world. However, it's still not part of universal screening programme in most of the countries.

Routine examination of newborn remains a poor screening tool to detect CHDs soon after birth when cyanosis could be difficult to detect with naked eyes and clinical signs of CHDs are often absent. Fetal

anomaly screening has now become an established screening tool to detect CHDs in most of the developed countries.

### What is fetal anomaly screening?

Fetal anomaly screening is an ultrasound scan done to detect major congenital malformations in the fetus. The detection rate of these malformations may vary depending upon the pathology, technical challenge and experience of the sonographer.

The cardiac anomalies which are currently being screened for include: dextrocardia, common arterial trunk, significant atrioventricular septal defect (AVSD), significant ventricular septal defect (VSD), simple transposition of great arteries (TGA), tetralogy of Fallot and hypoplastic left heart.

Fetal anomaly screening is routinely offered to all pregnant women in the United Kingdom between 18+0 weeks and 20+6 weeks of pregnancy under the National Health Service (NHS) Fetal Anomaly Screening Programme (FASP). FAS incorporates ultrasound visualisation of the heart aiming to identify structural abnormalities. Traditionally, the four-chamber view has been used in FAS to visualise the fetal heart. The atria and ventricles, interventricular septum, foramen ovale, and atrioventricular valves can all be assessed using this view.

Abnormality	Target detection rate
Anencephaly	100%
Open spina bifida	90%
Cleft lip	75%
Diaphragmatic hernia	60%
Gastroschisis	100%
Exomphalos	80%
Cardiac anomaly*	60%
Bilateral renal agenesis	85%
Lethal skeletal dysplasia	60%

**Table 1:** Showing target detection rate of abnormalities on the fetal anomaly screening in the UK.

However, results from a multitude of studies suggest that the four-chamber view used alone identifies less than 50% of patients with critical CHDs. Notably, it has been estimated that an abnormal four chamber view is only associated with an abnormality of the great

vessels in about 30% of cases [1]. Now, the International Society for Ultrasound in Obstetrics and Gynaecology (ISUOG), Royal College of Obstetrics and Gynaecology (RCOG) and National Institute of Clinical Excellence (NICE) guidelines all recommend both four-chamber and outflow tract views of the heart as part of FAS [2] (<https://www.gov.uk/government/publications/fetal-anomaly-screening-programme-standards>).

This increases the probability of identifying CHDs involving abnormalities of the outflow tracts (including transposition of the great arteries [TGA], tetralogy of Fallot, and double outlet right ventricle [DORV]). A significant improvement in the antenatal detection rate of significant CHD can be achieved when a concerted effort is made to visualise the outflow tracts [3].

Colour Doppler may also be employed to aid visualisation of normal anatomy, septal defects, and abnormal patterns of blood flow, associated for example with complex heart defects, valvular stenosis, coarctation, and hemodynamic compromise such as regurgitation and poor contractility. This may improve detection of CHD [4] (Table 1).

### Prenatal detection of congenital heart defects on FAS

CHDs with a reasonable probability of being visualised using the four-chamber and outflow tract views are listed in Table 2.

A number of structural cardiac abnormalities are difficult to identify even by an experienced ultrasonographer. These include total anomalous pulmonary venous connections (TAPVC), small or moderate sized muscular VSDs, milder forms of aortic coarctation, and mild aortic and pulmonary valve stenosis.

Four-Chamber View	
Septal defects	Significant atrioventricular septal defect (AVSD)
	Significant ventricular septal defect (VSD)
Left Heart Abnormalities	Hypoplastic left heart
	Critical aortic stenosis
	Severe coarctation of aorta
Right Heart Abnormalities	Tricuspid atresia
	Pulmonary atresia with intact ventricular septum
	Ebstein's anomaly
Double Inlet Ventricles	Double inlet left or right ventricle
Outflow Tract Views	
	Transposition of great arteries
	Tetralogy of Fallot or pulmonary atresia
	Truncus arteriosus
	Significant double outlet right ventricle (DORV)
	Severe coarctation of aorta

**Table 2:** Showing detection of cardiac anomalies on different views during fetal anomaly screening.

Furthermore, it must be remembered that certain CHDs are normal during fetal life, including patent ductus arteriosus and secundum-type atrial septal defects, therefore precluding antenatal detection.

Additionally, some CHDs may not be detectable in the second trimester owing to their development pattern. For instance, hypoplastic left heart syndrome (HLHS) may initially arise as left outflow tract stenosis, with left ventricle hypoplasia appearing only later on.

### Antenatal detection rates of CHDs on fetal anomaly screening

Whilst rates of prenatal diagnosis have steadily been increasing both nationally (Table 3) and internationally, the overall antenatal detection rate of CHD in the UK remains low, averaging 30-60%. Figure 1 below outlines regional variations in antenatal diagnostic rates of CHD across the UK for data collected by the National Institute for Cardiovascular Outcomes Research (NICOR) for the year 2013-2014. The mean antenatal diagnostic rate for CHD for the whole UK during the same period was 45.7%.

Data collected for the British Congenital Cardiac Association in 2007 suggested that antenatal detection of CHD is higher in London and the South East than elsewhere, with 50-55% of infants diagnosed prenatally in paediatric cardiology centres within London and south England versus 20-30% in centres outside London.

Similarly, a recent large USA-wide study looking at over 30000 infants and neonates undergoing surgery for CHD identified an overall prenatal detection rate of 34%, with an increase every year from 26% in 2006 to 42% in 2012, and a significant variation in rates across states ranging from 11.8% to 53.4% [5].

Despite relatively low rates of antenatal diagnosis, there is good evidence that screening programmes such as the FASP significantly increase antenatal detection of CHD. In the UK, introduction of a four-chamber view training programme in the South East Thames Region between 1988-1991 resulted in an increase in the antenatal detection rate of CHDs producing an abnormal four-chamber view from 3% to 67% at participating centres [6]. A recent study evaluating the effectiveness of a national prenatal screening programme introduced in the Netherlands in 2007 found an increase in the detection rate of severe CHD from 35.8 to 59.7% after the screening was introduced, with a corresponding reduction in the proportion of late referrals [7].

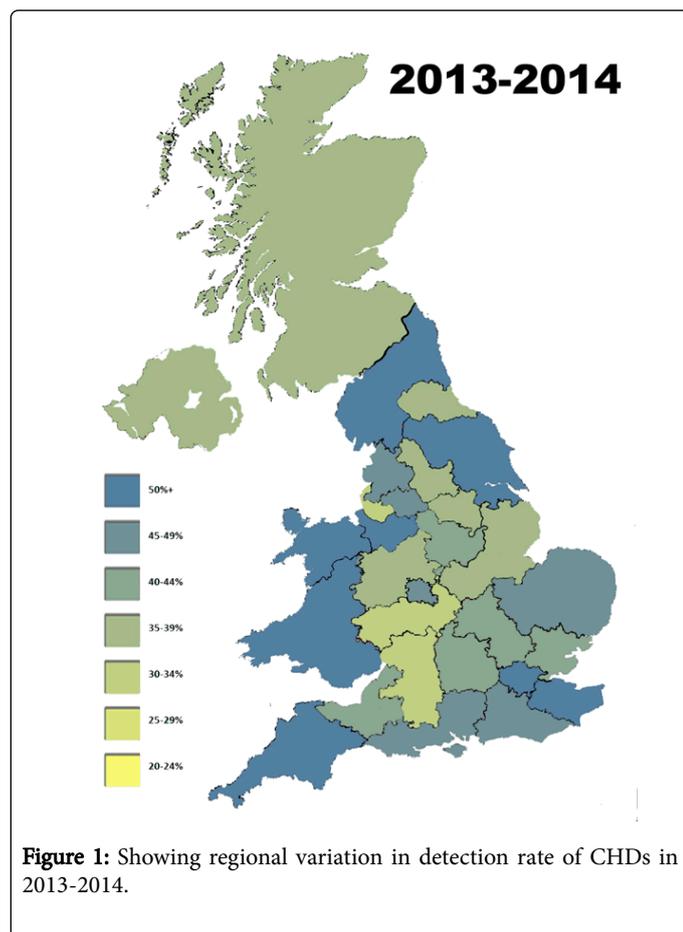
Detection rates vary by type of CHD, typically lower for lesions affecting the outflow tracts than lesions visible in the four-chamber view. A retrospective study carried out in Utah, USA looking at data from 1997-2007 identified that defects that would be expected to have an abnormal outflow-tract view were missed more frequently (64%) than were those that would be expected to have an abnormal four-chamber view (42%) [8]. Nonetheless, there is some evidence that antenatal diagnostic rates for lesions affecting the outflow tracts are increasing, with a recent study reported a substantial increase in the antenatal detection rate of TGA over a 20 year period [9].

Prenatal ultrasonography displays a predilection for identifying more severe cardiac lesions. A study carried out in the Czech Republic using data collected over a 21 year period from the nationwide prenatal ultrasound screening programme identified that around one third of all CHD was detected antenatally, rising to 80% when only critical forms were considered. There was a substantial contrast in antenatal detection rates between conditions, exemplified by a 95.8% detection rate for HLHS in recent years, versus 25.6% for TGA [10].

A multitude of studies have reported that antenatal detection rates of CHD are higher in tertiary and university centres than community-based centres [11]. In extension, the prevalence of disease within a population influences the sensitivity of any screening tool – specialist centres will see more foetuses with CHD since they are the centres to which women with indications for fetal echocardiography (Box 3) are referred. Accordingly, CHD prevalence in specialist centres has been found to be twice that expected in the general population [12].

	2009-10	2010-11	2011-12
England	3100%	33	35
Northern Ireland	3600%	32	
Scotland	2900%	23	36
Wales	3400%	42	52
UK	3100%	33	35

**Table 3:** Showing national detection rates of CHDs in the UK.



### Challenges in FAS: reasons for low antenatal detection rates and potential for improvement

There are a number of frequently cited reasons for low antenatal diagnosis rates. A major factor is the training and clinical expertise of ultrasonographers. It has been demonstrated that both the ability to successfully visualise the fetal heart and the antenatal detection rate of

major CHDs are significantly influenced by the experience of sonographers/midwives [13]. Furthermore, there is evidence that a simple training programme for obstetric ultrasonographers increased their ability to detect serious CHD [14]. It is thus paramount to the success of antenatal screening programmes that ultrasonographers are supported in their training. A number of international organisations are aiming to improve antenatal diagnosis rates of CHD in the future by standardising and auditing FAS teaching and training.

Several maternal/fetal factors also influence the ability to visualise the fetal heart. These include fetal position, amniotic fluid volume, maternal body habitus, and previous abdominal surgery.

A key factor in maximising antenatal detection rates in the general population is the maintenance of a record of CHD cases for the purpose of internal auditing and comparing the performance of different centres involved in screening. In the UK, NICOR provides a record of CHD diagnoses and outcomes for infants who undergo CHD surgery. Investigators manually linked NICOR data on antenatal diagnoses of CHD with data from maternity records to evaluate the performance of different centres in antenatal detection of CHD [15].

### Fetal Echocardiography

Where CHD is suspected on FAS, a referral should be made to a fetal cardiologist for a definitive diagnosis, counselling and CHD management. Indeed, suspected cardiac abnormality on FAS is one of the most common indications for referral for fetal echocardiography (Table 4). Given the high sensitivity of detailed fetal echocardiography in identifying cardiac abnormalities, it has been suggested that this itself might be used as screening tool to increase the antenatal detection rate of CHDs. However, current evidence points to a high cost associated with screening echocardiography as well as a false positive rate of around 5% [16], which might lead to undue parental anxiety.

### Significance of antenatal detection of CHDs: Why to bother?

One of the seven criteria outlined by Wilson and Jungner in assessing the validity of a screening programme is the availability of effective treatment in the event of a positive finding [17]. It is therefore pertinent to assess the reported benefits that accompany an antenatal diagnosis of CHD.

Firstly, an antenatal diagnosis permits the clinician to counsel parents regarding the diagnosis, prognosis and management of CHD. If appropriate, a referral can be made to identify any co-existing chromosomal or extra-cardiac abnormalities. Parents may use this information to decide whether or not to terminate the pregnancy, and if they choose to continue the pregnancy they would be better prepared for what the future is likely to hold for themselves and their child.

An antenatal diagnosis of CHD permits development of a perinatal management plan to support the pregnant mother and neonate in order to optimise outcomes, including by arranging for delivery (timing, mode, location) to take place in a specialist centre with appropriate facilities and expertise to manage the neonate with CHD. Evidence suggests that an antenatal diagnosis of CHD and the resultant early specialist management reduce perinatal morbidity in the pre-operative period and produce positive neurodevelopmental outcomes [18].

Fetal indications	
	· Suspicion of CHD on FAS
	· Increased nuchal translucency thickness in first trimester
	· Major extra-cardiac abnormality
	· Fetal hydrops
	· Fetal arrhythmias
	· Abnormal fetal karyotype: Trisomies 13, 18, 21; Turner syndrome; DiGeorge syndrome
	· Monochorionic pregnancy: Risk of cardiac abnormality or twin–twin transfusion syndrome
	· Increased risk of fetal heart failure, such as absent ductus venosus, fetal anaemia, or presence of fetal tumours with large vascular supply
	· History of CHD in a first-degree relative
Maternal indications	
	· Teratogenic drugs: Retinoids, lithium, anticonvulsants, amphetamines
	· Maternal alcohol abuse
	· Metabolic disease: DM, Phenylketonuria
	· Maternal infection: Rubella, Coxsackie, Parvovirus
	· Maternal antibody status, such as positive anti-Ro, anti-La antibodies
	· Increased maternal risk for Down's syndrome and other congenital defects (advanced maternal age or increased risk of Down's syndrome on serum screening)
	· Familial inherited disorders (e.g. Marfan syndrome)
	· Assisted conception or in vitro fertilisation

**Table 4:** Showing indications of fetal echocardiography.

There is strong evidence to support the view that an antenatal diagnosis of CHD reduces the need for emergency interventions in the neonate. A recent UK-based study by Peake et al. reported that the risk of postnatal intubation was reduced when HLHS and TGA were diagnosed prenatally [19]. Another study found that antenatally diagnosed patients were less likely to require mechanical ventilation and received earlier balloon atrial septostomy. Antenatally diagnosed infants are also less likely to require emergency surgery [20].

Furthermore, there is some evidence supporting the notion that antenatal diagnosis reduces mortality in HLHS, coarctation of the aorta, and TGA [20-23]. However, the fact that the fetal spectrum of CHDs is shifted towards complex lesions and those with associated chromosomal and extra-cardiac abnormalities means that a number of studies have identified poorer survival in infants diagnosed antenatally compared with those diagnosed postnatally. Exemplifying this notion, one study found that one year survival rate was significantly lower for infants with critical CHD diagnosed antenatally compared to those diagnosed postnatally (77% versus 96%), whereas this was not the case for non-critical CHDs, which the authors proposed reflected more severe disease among the critical CHD subtypes diagnosed antenatally [24]. Further, difficulty arises when comparing outcomes following antenatal versus postnatal diagnosis by virtue of the fact that those with a postnatal diagnosis have already survived fetal life and often the early neonatal period, such that the cohort as a whole demonstrates a survival advantage relative to those diagnosed prenatally.

For severe CHDs with potential for rapid deterioration during the gestational period and immediately following birth, there is potential for intervention in utero. The major focus in this regard has been severe aortic stenosis, which can evolve into HLHS at birth. In a study of 70 fetuses who underwent aortic balloon valvuloplasty in utero, the procedure was deemed to be technically successful in 52 (74%) [25].

There is also evidence that a prenatal diagnosis of CHD reduces the need to transfer infants large distances to specialist cardiac centres and reduces the associated costs, since the perinatal management plan will include planning for a suitable delivery location. Gupta et al. 2014 also found that prenatally diagnosed infants displayed reduced transfer distance, were less likely to require 'time-critical' transport, had reduced requirement for cardiorespiratory support (invasive intubation and inotrope use) during transport, and had shorter first hospital stays [26].

Morris et al. found that infants with HLHS born far from a cardiac surgical centre have greater neonatal mortality, which predominantly occurred prior to surgery [27]. A supported approach for delivering antenatally diagnosed infants (excluding HLHS and TGA, who are preferably delivered in or near the paediatric cardiology centre) at tertiary neonatal centres outside paediatric surgical centre could have equally better outcome, providing there is sufficient expertise, careful multi-disciplinary planning, and good communication with a specialist cardiac centre [28].

## Conclusion

Fetal anomaly screening is an excellent tool to detect critical and significant congenital heart defects prenatally. Antenatal diagnosis helps in clinical decision making and planning of delivery, preparing parents for anticipated problems and improves outcome for infants with CHDs. However, despite the advancement in technology and training rate of antenatal detection remains low. Outflow tract and three vessels view have improved detection rate. Some of the CHDs (like coarctation of aorta) are notoriously difficult to diagnose antenatally. Reinforcement of high quality training in fetal anomaly screening and robust clinical governance to monitor detection of CHDs are crucial in continually improving the detection rate.

## References

1. Paladini D, Rustico M, Todros T, Palmieri S, Gaglioti P, et al. (1996) Conotruncal anomalies in prenatal life. *Ultrasound Obstet Gynecol* 8: 241-246.
2. The International Society of Ultrasound in Obstetrics (2013) ISUOG Practice Guidelines (updated): sonographic screening examination of the fetal heart. *Ultrasound Obstet Gynecol* 41: 348-359.
3. Levy DJ, Pretorius DH, Rothman A, Gonzales M, Rao C, et al. (2013) Improved prenatal detection of congenital heart disease in an integrated health care system. *Pediatr Cardiol* 34: 670-679.
4. Eggebo TM, Heien C, Berget M, Ellingsen CL (2012) Routine use of color Doppler in fetal heart scanning in a low-risk population. *ISRN Obstet Gynecol* 2012: 496935.
5. Quartermain MD, Pasquali SK, Hill KD, Goldberg DJ, Huhta JC, et al. (2015) Variation in Prenatal Diagnosis of Congenital Heart Disease in Infants. *Pediatrics* 136: e378-385.
6. Sharland GK, Allan LD (1992) Screening for congenital heart disease prenatally. Results of a 2 1/2-year study in the South East Thames Region. *Br J Obstet Gynaecol* 99: 220-225.
7. van Velzen CL, Clur SA, Rijlaarsdam M, Bax CJ, Pajkrt E, et al. (2016) Prenatal detection of congenital heart disease-results of a national screening programme. *BJOG* 123: 400-407.
8. Pinto NM, Keenan HT, Minich LL, Puchalski MD, Heywood M, et al. (2012) Barriers to prenatal detection of congenital heart disease: a population-based study. *Ultrasound Obstet Gynecol* 40: 418-425.
9. Escobar-Diaz MC, Freud LR, Bueno A, Brown DW, Friedman KG, et al. (2015) Prenatal diagnosis of transposition of the great arteries over a 20-year period: Improved but imperfect. *Ultrasound Obstet Gynecol* 45: 678-682.
10. Marek J, Tomek V, Skovránek J, Povysilová V, Samánek M (2011) Prenatal ultrasound screening of congenital heart disease in an unselected national population: a 21-year experience. *Heart* 97: 124-130.
11. Friedberg MK, Silverman NH, Moon-Grady AJ, Tong E, Nourse J, et al. (2009) Prenatal detection of congenital heart disease. *J Pediatr* 155: 26-31.
12. Buskens E, Stewart PA, Hess J, Grobbee DE, Wladimiroff JW (1996) Efficacy of fetal echocardiography and yield by risk category. *Obstet Gynecol* 87: 423-428.
13. Tegnander E, Eik-Nes SH (2006) The examiner's ultrasound experience has a significant impact on the detection rate of congenital heart defects at the second-trimester fetal examination. *Ultrasound Obstet Gynecol* 28: 8-14.
14. Hunter S, Heads A, Wyllie J, Robson S (2000) Prenatal diagnosis of congenital heart disease in the northern region of England: benefits of a training programme for obstetric ultrasonographers. *Heart* 84: 294-298.
15. Gardiner HM, Kovacevic A, van der Heijden LB, Franklin RCG, et al. (2013) Prenatal screening for major congenital heart disease: assessing performance by combining national cardiac audit with maternity data. *Heart* 100: 375-382.
16. Knowles R, Griebsch I, Dezateux C, Brown J, Bull C, et al. (2005) Newborn screening for congenital heart defects: a systematic review and cost-effectiveness analysis. *Health technology assessment* 9: 1-152.
17. Wilson JM, Jungner YG (1968) [Principles and practice of mass screening for disease]. *Bol Oficina Sanit Panam* 65: 281-393.
18. Fuchs IB, Muller H, Abdul-Khaliq H, Harder T, Dudenhausen JW, et al. (2007) Immediate and long-term outcomes in children with prenatal diagnosis of selected isolated congenital heart defects. *Ultrasound Obstet Gynecol* 29: 38-43.
19. Peake LK, Draper ES, Budd JL, Field D (2015) Outcomes when congenital heart disease is diagnosed antenatally versus postnatally in the UK: a retrospective population-based study. *BMC Pediatr* 15: 58.
20. Levey A, Glickstein JS, Kleinman CS, Levasseur SM, Chen J, et al. (2010) The impact of prenatal diagnosis of complex congenital heart disease on neonatal outcomes. *Pediatr Cardiol* 31: 587-597.
21. Connor JA, Thiagarajan R (2007) Hypoplastic left heart syndrome. *Orphanet J Rare Dis* 2: 23.
22. Franklin O, Burch M, Manning N, Sleeman K, Gould S, et al. (2002) Prenatal diagnosis of coarctation of the aorta improves survival and reduces morbidity. *Heart* 87: 67-69.
23. Bonnet D, Coltri A, Butera G, Fermon L, Le Bidois J, et al. (1999) [Prenatal diagnosis of transposition of great vessels reduces neonatal morbidity and mortality]. *Arch Mal Coeur Vaiss* 92: 637-640.
24. Oster ME, Kim CH, Kusano AS, Cragan JD, Dressler P, et al. (2014) A population-based study of the association of prenatal diagnosis with survival rate for infants with congenital heart defects. *Am J Cardiol* 113: 1036-1040.
25. McElhinney DB, Marshall AC, Wilkins-Haug LE, Brown DW, Benson CB, et al. (2009) Predictors of technical success and postnatal biventricular outcome after in utero aortic valvuloplasty for aortic stenosis with evolving hypoplastic left heart syndrome. *Circulation* 120: 1482-1490.
26. Gupta N, Leven L, Stewart M, Cheung M, Patel N (2014) Transport of infants with congenital heart disease: benefits of antenatal diagnosis. *Eur J Pediatr* 173: 655-660.
27. Morris SA, Ethen MK, Penny DJ, Canfield MA, Minard CG, et al. (2014) Prenatal diagnosis, birth location, surgical center, and neonatal mortality in infants with hypoplastic left heart syndrome. *Circulation* 129: 285-292.
28. Anagnostou K, Messenger L, Yates R, Kelsall W (2013) Outcome of infants with prenatally diagnosed congenital heart disease delivered outside specialist paediatric cardiac centres. *Arch Dis Child Fetal Neonatal Ed* 98: 218-221.