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Knowledge And Perception Of The Role Of Targeted Ultrasound In Detecting Down Syndrome Among A High Risk Population

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KNOWLEDGE AND PERCEPTION OF THE ROLE OF TARGETED ULTRASOUND IN DETECTING DOWN SYNDROME AMONG A HIGH RISK POPULATION

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A

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The purpose of this study was to determine the perception and knowledge of targeted ultrasound in women who screen positive for Down syndrome in the first or second trimester, and to assess the perceived detection rate of Down syndrome by targeted ultrasound in this population. While several studies have reported patient perceptions' of routine ultrasound, no study has specifically examined knowledge regarding the targeted ultrasound and its role in detecting Down syndrome. A targeted ultrasound is a special ultrasound during the second trimester offered to women who may be at a higher-than-average risk of having a baby with some type of birth defect or complication. The purpose of the ultrasound is to evaluate the overall growth and development of the baby as well as screen for birth defects and genetic conditions. Women under the age of 35 referred for an abnormal first or second trimester maternal serum screen to several Houston area clinics were asked to complete a questionnaire to obtain demographic and ultrasound knowledge information as well as assess perceived detection rate of Down syndrome by ultrasound. Seventy-seven women completed the questionnaire and participated in the study.

Our findings revealed that women have limited background knowledge about the targeted ultrasound and its role in detecting Down syndrome. These findings are consistent with other studies that have reported a lack of understanding about the purpose of ultrasound

examinations. One factor that seems to increase background knowledge about the targeted ultrasound is individuals having a higher level of education. However, most participants regardless of race, education, income, and exposure to targeted ultrasound information did not know the capabilities of a targeted ultrasound.

This study confirmed women lack background knowledge about the targeted ultrasound and do not know enough about the technology to form a perception regarding its ability to detect Down syndrome. Additional studies to identify appropriate education techniques are necessary to determine how to best inform our patient population about targeted ultrasound.

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Introduction

Prenatal diagnosis of chromosome abnormalities has become increasingly more common with the delay of childbearing in women into their mid to late thirties and early forties (Milunsky & Milunsky, 2010). Due to the associated risk of miscarriage with prenatal diagnostic procedures, the risk for fetal loss is increasingly regarded as unacceptable. Researchers strive to develop techniques that optimize selection of pregnancies warranting invasive testing to decrease procedure-related losses of normal fetuses (Yeo & Vintzileos, 2003). The goal of targeted sonography is to evaluate for mid-trimester markers allowing the practitioner to adjust the risk of fetal aneuploidy (Bahado-Singh, Oz, Mendilcioglu, & Mahoney, 2005). Due to varied midtrimester presentation, maternal body habitus, ultrasonographic markers, operator proficiency, and available equipment, detection rate of fetal aneuploidy by ultrasound, primarily trisomy 21, is dependent on several factors and the efficacy is controversial. Genetic counseling is an important step in educating patients on the benefits, risks and limitations of ultrasound. The purpose of this study is to determine perception and knowledge of targeted ultrasound in women who screen positive for Down syndrome in the first or second trimester and to assess the perceived detection rate of Down syndrome by targeted ultrasound in this population.

Down Syndrome

Down syndrome is one of the most common genetic conditions and occurs with a frequency of 1 in 800 live births per year in the United States (Nussbaum, McInnes, Willard,

Thompson, & Hamosh, 2007). Individuals with Down syndrome have some degree of mental retardation and characteristic facial features. Health concerns among individuals with Down syndrome are more frequent than that in the general population, although severity and frequency are variable (March of Dimes, 2009).

The increased health problems and mental retardation are due to an extra copy of chromosome 21. Forty-four percent of individuals with Down syndrome have a congenital heart defect, most commonly atrioventricular septal defect, secundum atrial septal defect, and ventral septal defect (Freeman et al., 2008). Seventy-five percent will have some form of hearing loss, and there is a high incidence of otitis media (50-70%) and eye disease (60%) as well. Additional health conditions may include Hirschsprung disease, leukemia, sleep apnea, congenital hypothyroidism and an increased incidence of early onset Alzheimer disease ("American Academy of Pediatrics: Health supervision for children with Down syndrome," 2001; Tyrrell et al., 2001). The degree of mental retardation is variable ranging from mild (Intellectual Quotient (IQ) 50-70) to moderate (IQ 35-50), and in rare cases, severe mental impairment may occur (IQ 20-35) ("American Academy of Pediatrics: Health supervision for children with Down syndrome," 2001).

An association between maternal age and an increased risk for Down syndrome is well established. Advanced maternal age is defined as a woman who is 35 years of age or older at the time of delivery. The mid-trimester risk for Down syndrome for a 35-year-old woman is 1 in 250 (Hook, 1981). Traditionally, women of advanced maternal age are considered at “high risk,” and those below this threshold are considered “low risk” (Bromley, Lieberman, Shipp, & Benacerraf, 2002). Although the risk for Down syndrome increases with maternal age, 80% of infants born with Down syndrome are born to mothers

under the age of 35, as women in this age group have a higher frequency of births in general (National Down Syndrome Congress, 2010). Maternal age as a screening method currently identifies only about 47% of trisomy 21 cases and is associated with a high false-positive rate (12%-13%) (Egan et al., 2000). For these reasons, maternal age alone is not the most optimal screening tool (Driscoll & Gross, 2009). Maternal serum screening is often utilized to categorize women under the age of 35 years whose pregnancies are at an increased risk for Down syndrome; moving them from a low risk to a high risk category.

Prenatal Screening

The association between maternal age and incidence of Down syndrome has triggered the use of prenatal serum screening and diagnostic testing to identify pregnancies at higher risk for karyotypic abnormalities. Currently, the American College of Obstetricians and Gynecologists (ACOG) recommends that all women, regardless of age, be offered screening tests for aneuploidy prior to 20 weeks gestation ("ACOG Practice Bulletin No. 77: Screening for fetal chromosomal abnormalities," 2007). Maternal serum screening, apart from maternal age, is the only screening method for Down syndrome and may be performed in the first or second trimester ("ACOG Educational Bulletin. Maternal serum screening," 1996). First trimester screening is performed between 11 and 14 weeks gestation and consists of a sonographically obtained nuchal translucency measurement combined with maternal serum free beta human chorionic gonadotropin (hCG) and pregnancy-associated plasma protein-A (PAPP-A) measurements and maternal age (March of Dimes, 2008). The detection rate for Down syndrome by first trimester screening ranges from 82% to 87% ("ACOG Practice Bulletin No. 77: Screening for fetal chromosomal

abnormalities," 2007). Second trimester screening tests are performed between 15 and 20 weeks gestation (March of Dimes, 2008). These tests include triple (maternal serum alpha-fetoprotein (MSAFP), hCG, and unconjugated estriol), quadruple (includes inhibin A in addition to triple markers), or penta (includes invasive trophoblast antigen or ITA) marker screening in conjunction with maternal age. The detection rates for Down syndrome by these screening tests are 69%, 81%, and 83%, respectively ("ACOG Practice Bulletin No. 77: Screening for fetal chromosomal abnormalities," 2007; Palomaki, Neveux, Knight, Haddow, & Pandian, 2004). It is essential for patients to understand the difference between a screening test and a definitive diagnostic test with its associated risks, and the benefits and limitations of each procedure.

Diagnostic Tests

Invasive testing for prenatal diagnosis includes chorionic villus sampling (CVS), offered between 10 and 13 weeks-gestation, amniocentesis, offered after 15 weeks-gestation, and fetal blood sampling. The risk for miscarriage due to CVS is approximately 0.5% to 1%, while the average risk associated with amniocentesis is 0.25% to 0.5% ("Chorionic villus sampling and amniocentesis: recommendations for prenatal counseling. Centers for Disease Control and Prevention," 1995). More recently, ACOG reports the procedure-related risk with amniocentesis as being between 0.2% to 0.33% ("ACOG Practice Bulletin No. 88, December 2007. Invasive prenatal testing for aneuploidy," 2007).

Prior to 2007, ACOG only recommended offering diagnostic testing to women of advanced maternal age, or those considered at increased risk due to abnormal serum screen results, due to the procedural risk for miscarriage ("ACOG Practice Bulletin No. 77:

Screening for fetal chromosomal abnormalities," 2007). ACOG now recommends that all pregnant women should have the option of diagnostic testing in addition to, or in lieu of, screening regardless of age or screening results ("ACOG Practice Bulletin No. 77: Screening for fetal chromosomal abnormalities," 2007). Prior to the 1950's, amniocentesis was indicated for the treatment of hydramnios during pregnancy. It was also used to localize the placenta by contrast media injection, during pregnancy termination by injection of hypertonic saline, and for monitoring of fetuses with Rh isoimmunization. Since that time, advancements in prenatal diagnosis have allowed for prenatal detection of chromosome disorders and other genetic conditions via traditional amniocentesis and chorionic villus sampling (Milunsky & Milunsky, 2010). Early amniocentesis, performed prior to 15 weeks gestation, is not offered clinically on a regular basis unless a lethal anomaly is suspected due to incomplete fusion of amniotic and chorionic membranes, a higher rate of spontaneous pregnancy loss and an increased rate of talipes equinovarus (Milunsky & Milunsky, 2010).

Because the majority of pregnancies subjected to the miscarriage risks associated with invasive testing are chromosomally normal, the risk for fetal loss is increasingly regarded as unacceptable. There is a rising demand for the combined evaluation of maternal age, maternal serum screening, and ultrasound findings to determine individualized patient risk estimates to more accurately identify pregnancies warranting invasive testing (Breathnach, Fleming, & Malone, 2007).

Ultrasound Technology

Ultrasound is a significant advancement in prenatal diagnosis and management. Prenatal sonographic imaging continues to improve and has become a widely used screening

tool for pregnant women, including those at low risk (Verrotti, Caforio, Gramellini, & Nardelli, 2007). Approximately 70% of pregnant women in the United States have an ultrasound exam at least once during pregnancy (Martin et al., 2003).

Ultrasound was introduced as a diagnostic tool in medicine in the early 1940's. Prior to 1975, ultrasound was used in obstetric medicine for biparietal diameter, determination of amniotic fluid volume, evaluation of singleton or multiple gestations, intrauterine fetal death, and placental location. The first real-time scanners were developed in the late 1960's enabling visualization of fetal movement and more accurate diagnosis of several fetal abnormalities. Malformations including anencephaly, duodenal atresia, hydrops fetalis, bone dysplasias, hydrocephalus, and polycystic kidneys were clearly diagnosed via ultrasound by the early 1980's. With improvements in technology, including high resolution scanners, the diagnosis of spina bifida and other more subtle abnormalities, such as cardiac defects, became possible. Current technology allows diagnosis of fetal anomalies earlier in gestation; moving prenatal diagnosis from the third trimester to the second, and sometimes to the first trimester. With current ultrasound equipment, sonographers and sonologists are capable of identifying minor fetal abnormalities and normal variants known as soft signs or soft markers associated with chromosome abnormalities (Woo, 2001).

Ultrasound technology continues to evolve and improve supporting more accurate fetal observation and diagnosis. Color flow Doppler and power Doppler imaging were developed to examine fetal circulation and measure fetal, placental, and umbilical cord blood flow velocities. Introduction of three-dimensional ultrasound provides additional scan planes to better evaluate fetal anomalies, particularly after post processing analysis. One of

the greatest advantages to this technology is its acceptance as a low-risk modality (Twining, 2000).

In general, ultrasound is a noninvasive, sound wave imaging tool generated by a transducer attached to a hand-held probe. The most advanced ultrasound technology employs a method using synthetic crystals (zirconate) to provide low-energy, high-frequency sound waves. Waves of low and high pressure vibrations are created and transmitted into the tissue. In order to obtain the image, a coupling gel is applied to the transducer to decrease the loss of sound waves at the skin-transducer interface. The gel eliminates air between the probe and surface of skin. The waves reflect off of fetal and maternal tissues and are detected by the emitting transducer. The image produced is displayed on a screen corresponding to the intensity of the echo. There are 128 intensity or brightness shades shown on a gray scale. Blood, amniotic fluid, and urine appear black on the ultrasound screen as sound waves pass through liquid and do not reflect back. Denser tissues, such as bone, absorb the sound wave and appear white or echogenic. Soft tissues appear as shades of gray depending on the density. The resulting image is also dependent on the time lag of the returning echo. The majority of diagnostic ultrasounds today operate by a phased array real-time technology. Motion of the target structure, as seen in real-time ultrasonography, is possible due to sequential firing of multiple crystals. This allows ultrasound waves to emit and receive fast enough to detect movement (Creasy & Resnik, 1994; Cunningham & Williams, 2001).

There are four distinct types of ultrasound examinations as defined by ACOG. First trimester ultrasound is performed prior to 13 weeks and 6 days gestation and primarily confirms intrauterine pregnancy viability, gestational age, and diagnosis of multiple

gestations. Additionally, first trimester ultrasounds are utilized for nuchal translucency measurements for first trimester aneuploidy screening. The standard obstetric ultrasound exam is performed during the second or third trimester and evaluates fetal presentation, volume of amniotic fluid, cardiac activity, placental position, fetal number, and basic fetal anatomy. A limited ultrasound examination is used to assess a specific question, such as confirming fetal heart rate or placental location and is usually performed after a standard exam is on file. Finally, the specialized exam, also known as the targeted ultrasound, is similar to the standard obstetric ultrasound but assesses fetal anatomy in detail and is often performed when an anomaly is suspected ("ACOG Practice Bulletin No. 101: Ultrasonography in pregnancy," 2009).

Ultrasound is a screening tool limited primarily by gestational age and technology (Bofill & Sharp, 1998). Bofill and Sharp (1998) describe two of the pitfalls associated with antenatal sonograms: misdiagnosis and missed diagnosis. Misdiagnosis is a false-positive scan and often corrected by a follow-up, more detailed sonogram performed at a tertiary care center. A missed diagnosis, or false-negative scan, will not be detected unless further examination is pursued for an additional indication.

Women with certain indications, or high risk populations, are referred for targeted sonograms which are ideally performed during the second trimester. Indications for a targeted ultrasound include abnormalities in amniotic fluid volume, abnormal maternal serum screen results, advanced maternal age, family or personal history of a chromosome abnormality or birth defect, teratogen exposure, structural anomalies identified on prior obstetrical scan, or maternal illness (Bofill & Sharp, 1998). Among high risk populations, the term “genetic sonogram” evolved to describe the application of the targeted, second

trimester ultrasound to adjust the risk for chromosomal aneuploidy (Breathnach et al., 2007). Both structural anomalies and sonographic markers, or soft signs, are used to evaluate the risk for aneuploidy.

The use of ultrasound in prenatal diagnosis for structural malformations is highly dependent on operator expertise. Structural malformations frequently identified in specialized centers include: central nervous system abnormalities such as anencephaly, spina bifida, and hydrocephalus, skeletal defects, and internal organ abnormalities. Detection of internal abnormalities such as congenital heart defects, renal anomalies, obstructive uropathy, abdominal wall defects, and fetal tumors, often depends on severity (Harper, 2004). As ultrasound is often most useful when interpreted in conjunction with other appropriate studies, further testing options should be considered in the context of suspected malformations.

Sonographic Findings for Down Syndrome

Both structural anomalies and soft sonographic markers can be combined to increase detection of chromosomal aneuploidy in a fetus. Unlike structural anomalies, soft markers are often clinically insignificant in isolation and may resolve over time. When screening for Down syndrome, the most common structural anomalies detected include cardiac defects, duodenal atresia, and cystic hygroma. Although it is possible to detect structural abnormalities in the late first trimester and early second trimester (Nyberg & Souter, 2001), most anomalies are not identified until further in gestation. Second trimester sonographic markers for Down syndrome include nuchal fold thickening, ventriculomegaly, short long

bones, echogenic bowel, pyelectasis, intracardiac echogenic focus, and hypoplastic nasal bone (Breathnach et al., 2007).

A fetus with trisomy 21 may not show structural abnormalities prior to 20 weeks (Nyberg & Souter, 2001). In a study performed by Nyberg and colleagues, major abnormalities were detected in 16.7% of fetuses with Down syndrome prior to 20 weeks gestation. This group excluded patients specifically referred for an identified structural malformation (Nyberg et al., 2001). Nearly 50% of babies with Down syndrome are born with a congenital heart defect (Freeman et al., 2008). Detecting heart defects by ultrasound depends on the type and severity of the defect and gestational age at the time of exam. Cardiac abnormalities are not readily identified at earlier gestational ages. An additional study of women at a mean gestational age of 16.9 weeks by Nyberg and colleagues consistently identified cardiac defects in less than 10% of fetuses with trisomy 21 (Nyberg & Souter, 2001). A comparable study evaluated women sonographically at a mean gestational age of 18 weeks with real-time and color Doppler ultrasound. Findings included structural and functional cardiac findings, such as ventral septal defects, outflow tract abnormalities, right-left disproportion, pericardial effusion, and tricuspid regurgitation. Seventy six percent of trisomy 21 fetuses had a heart finding, and only 9% were endocardial cushion defects. Although the study concentrated on heart findings associated with Down syndrome, multiple markers were evaluated. Excluding structural heart defects, the detection rate for Down syndrome was 60% but increased to 91% with inclusion of heart abnormalities. Therefore, identification of congenital cardiac defects is a major contributor to increased detection rate of Down syndrome by ultrasound (DeVore, 2000). Paladini and coworkers scanned 41 fetuses with a diagnosis of trisomy 21 at an average of 24 weeks in

pregnancy. With knowledge of fetal karyotype and at the optimal gestational age, about 50% of fetuses with Down syndrome studied had a detectable heart defect (Paladini et al., 2000). Other studies have reported higher detection of major malformations but often include patients referred for a previously identified anomaly which increases their detection rate.

Nyberg and collaborators reviewed common sonographic markers used to estimate risk of Down syndrome. Nuchal thickening refers to redundant skin at the back of the fetal neck. A measurement of 6 mm or greater after 15 weeks indicates an increased risk for trisomy 21 (Benacerraf, Frigoletto, & Laboda, 1985). Several studies, including the authors, use a cutoff of 5 mm at less than 20 weeks to increase detection and it only slightly increases the false-positive rate (Nyberg & Souter, 2001).

Hyperechoic bowel is often a benign finding but has shown an association with fetal aneuploidy defining it as a soft marker. A grading system is used to evaluate echogenic bowel. Grade 1 is mildly echogenic and often diffuse, grade 2 is moderately echogenic and typically focal, and grade 3 is very echogenic, as bright as bone. The authors consider both moderate and markedly hyperechoic bowel a risk factor for Down syndrome (Nyberg & Souter, 2001).

Generally, the size of the lateral cerebral ventricles does not change throughout gestation. The diameter measures 6.1 mm and varies slightly between male and female fetuses. Typically, males have larger ventricles than females (Patel, Goldstein, Tung, & Filly, 1995). Ventriculomegaly is defined when lateral ventricles measure 10 mm or greater. Mild ventriculomegaly is considered a minor marker for Down syndrome as it is often

transient and nonspecific, as well as a common characteristic identified in normal fetuses (Nyberg & Souter, 2001).

Short stature is a common feature in individuals with Down syndrome and is attributed to disproportionately short long bones: femur and humerus. Shortening of these bones can be detected prenatally. Measurements are evaluated by comparing the actual length with the expected length, typically based on biparietal diameter or a similar dating measurement as opposed to gestational age. Historically, single cutoff values were used for shortened femur and shortened humerus: 0.91 multiples of the median for short femur and 0.89 for short humerus (Nyberg & Souter, 2001). Recently, measurements of the long bones have been converted to expected multiple of the median data and calculated likelihood ratios rather than a universal cutoff (Bahado-Singh, Oz, Gomez et al., 1998).

Mild pyelectasis is most commonly seen in normal fetuses but shows an association with aneuploidy. Pyelectasis is defined as a measurement of the fluid-filled renal pelvis in an anteroposterior diameter above 4 mm in the mid-trimester (Nyberg & Souter, 2001).

The final common sonographic marker for Down syndrome is intracardiac echogenic foci (ICEF). ICEF refers to papillary muscle calcifications detected on ultrasound (Nyberg & Souter, 2001). Shipp et al. (Shipp, Bromley, Lieberman, & Benacerraf, 2000) found ICEF more common among Asian patients compared to Caucasian. Understanding the increased frequency in specific populations affects risk assessments for women with an identified ICEF (Nyberg & Souter, 2001).

Additional skeletal findings may be evaluated during ultrasound including clinodactyly (shortened middle phalanx of the fifth finger) and widened pelvic angle. These features are seen in some individuals with Down syndrome; however, both measurements

are difficult to assess by ultrasound and are often not included as screening markers (Nyberg & Souter, 2001). Absence of nasal bone is used in some centers.

Individual detection of soft markers varies by location, timing, and specific finding. Hobbins et al. (2003) evaluated a subgroup of 176 Down syndrome cases from a multi-center study referred during mid-trimester for advanced maternal age or an abnormal triple screen. This group evaluated the following sonographic markers shortened femur and humerus, increased nuchal skin thickness, pyelectasis, echogenic intracardiac focus, hypoplastic fifth digit, sandal gap toe, echogenic bowel, and the presence of major anatomical defects. Nuchal thickness had the highest sensitivity for detecting Down syndrome (36.5%). The sensitivity for other observed soft markers was short femur (20.6%), short humerus (20.6%), echogenic intracardiac focus (21.3%), pyelectasis (17.2%), hypoplastic fifth digit (18.9%), echogenic bowel (13.5%), and sandal gap toe (3%). The false-positive rates for this study were not reported. Interestingly, the sensitivity for AMA cases was reported as 70.8% (95/134) with varying estimates from 40-100%. Comparably, among the positive triple marker screen population, the sensitivity for Down syndrome was 71.4% (Hobbins et al., 2003).

Studies have also gathered information to calculate likelihood ratios (sensitivity/false-positive rate) of sonographic findings for fetal Down syndrome. The likelihood ratio for each soft marker reflects the associated risk for Down syndrome. Age-adjusted sonographic risk assessment includes the risk of the identified ultrasound findings by using the likelihood ratio (LR). The following table is data from Nyberg et al. (2001).

Sonographic Marker	LR Overall	LR for Marker as an Isolated Finding	95% Confidence Interval
Nuchal thickening	61	11	5.5-22
Hyperechoic bowel	33.8	6.7	2.7-16.8
Short humerus	15.3	5.1	1.6-16.5
Short femur	6.1	1.5	0.8-2.8
Echogenic intracardiac focus	6.3	1.8	1.0-3.2
Pyelectasis	5.2	1.5	0.6-3.6

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Smith-Bindman and colleagues determined likelihood ratios for sonographic markers and calculated similar values as Nyberg et al. (2001) and found the greatest likelihood ratio associated with nuchal thickening (LR=17). They concluded that as isolated findings, a second-trimester ultrasound soft marker is not useful in confirming or excluding the possibility of Down syndrome. Nuchal thickening is the only significant marker that may help to differentiate a fetus affected or unaffected (Smith-Bindman, Hosmer, Feldstein, Deeks, & Goldberg, 2001).

Sonographic soft markers in general appear more frequently among fetuses with a chromosomal anomaly compared to unaffected fetuses. Viora et al. reported a prevalence of soft markers in 70% of trisomy 21 cases compared to 28% of cases with normal karyotypes. They concluded that the clinical use of ultrasound in identifying pregnancies at risk for trisomy 21 using soft markers is limited by the high false-positive rate and low sensitivity (Viora, Errante, Bastonero, Sciarrone, & Campogrande, 2001). A meta-analysis of ultrasound markers in the mid-trimester to determine the accuracy of detecting Down syndrome prenatally produced similar results. A total of 56 articles were reviewed that included 1,930 cases of Down syndrome and 130,365 unaffected cases. The majority of the studies (88%) included women at high risk for chromosome abnormalities due to age, serum screening results, or a significant family history. Results showed that the sensitivity and

specificity for the detection rate of Down syndrome among the studies was highly variable. For example, the sensitivity for detecting fetuses with Down syndrome based on increased nuchal fold measurements ranged from 7% to 75%. The group determined two reasons for the heterogenous results. One, the accuracy of the studies was inconsistent based on the study design. There was a significant difference between studies performed by case-control or prospective methods. Second, sensitivity and specificity varied dependent on whether the marker was seen in isolation or with an associated structural anomaly. Studies evaluating Down syndrome risk based on isolated soft markers reported significantly lower sensitivities ranging from 1% for choroid plexus cysts to 16% for shortened femur. The review concluded that accuracy for most sonographic markers for Down syndrome is poor, but it remains common practice among clinicians to adjust risk for trisomy 21 based on these findings (Smith-Bindman et al., 2001).

Detection Rate of Down Syndrome by Ultrasound

As discussed, genetic sonography is the systematic use of multiple mid-trimester markers to adjust the risk of fetal aneuploidy. This type of ultrasound is historically used among high-risk pregnancies. While the frequency of major structural anomalies is much higher in trisomies 18 and 13 and ultrasound has a high sensitivity in detecting them (83-100% for trisomy 18 and 91% for trisomy 13), similar evidence for the effectiveness of identifying Down syndrome varies (Lehman et al., 1995; Nyberg et al., 1993). A review of literature revealed about 25% of second trimester fetuses with Down syndrome have distinctive ultrasound findings or structural malformations. Investigators have incorporated other soft markers to increase the sensitivity of ultrasound in the detection of Down

syndrome (Vintzileos & Egan, 1995). In addition, integrating ultrasound findings with other screening methods (i.e. biochemical serum markers and maternal age) increases the sensitivity for detecting Down syndrome (Bahado-Singh et al., 2005). For the purpose of this study, the value assigned to a positive genetic sonogram will be referred to as the detection rate of Down syndrome by ultrasound.

The detection rate of Down syndrome by ultrasound remains controversial and is variable. Quality of ultrasound equipment, technologist expertise, gestational age, maternal body habitus, fetal position, and the use of soft markers all play a role in the reported sensitivity. ACOG cites studies reporting a detection of malformations or soft markers suggestive of Down syndrome in approximately 50-75% of pregnancies during the second trimester but does not recommend using ultrasonography as a primary screening tool for Down syndrome due to its limitations ("ACOG Practice Bulletin No. 101: Ultrasonography in pregnancy," 2009). Although the sensitivity of screening methods does not match that of diagnostic testing options, the practice of offering routine invasive testing to all high risk pregnant women has been challenged due to the associated miscarriage risks. Efforts to improve sensitivity and specificity of screening tools are rapidly underway to minimize the number of women subjected to this risk. When advanced maternal age alone is used to categorize women into low and high risk, about 140 amniocenteses are required to identify one fetus with Down syndrome. When incorporating triple marker screening 60 amniocenteses are needed to detect one fetus with Down syndrome (Vintzileos & Egan, 1995). Using the definition of an abnormal genetic sonogram, Yeo and Vintzileos (2003) reviewed the accuracy of second-trimester genetic sonography for the detection of Down syndrome among several institutions. The overall sensitivity of the genetic sonogram was

77% and the false-positive rate was 13%. Vintzileos et al. (1996) reported a sensitivity of 93% (13/14) and a false-positive rate of 13% (54/406). Nyberg and coworkers evaluated 142 consecutive fetuses with trisomy 21 in the second trimester for nuchal thickening, echogenic bowel, shortened femur, shortened humerus, renal pyelectasis, and 'structural' abnormalities. The group published a sensitivity of 68.3% (97/142) and false-positive rate of 12.5% (116/930) for Down syndrome (Nyberg, Luthy, Resta, Nyberg, & Williams, 1998). Bromley et al. (1997) contributed to the literature with a reported sensitivity of 83% (44/53) and 17.5% false-positive rate (31/177) for the sonographic detection of Down syndrome. Using a similar panel of six ultrasound markers, one study found one or more abnormalities in 50% of pregnancies with Down syndrome (Nyberg et al., 1995). The variation between centers is a valid concern of ultrasound screening for Down syndrome. Based on the above criteria, any positive ultrasound finding increases the risk for aneuploidy. Many of the criteria used to evaluate the risk of trisomy 21 depend on measurements that reach a certain threshold. This becomes particularly sensitive within and between centers when measurements are of borderline significance. Small discrepancies in measurement can largely affect the risk assessment (Nyberg et al., 1998).

Of equal importance, a normal ultrasound scan can reduce the risk of Down syndrome when properly evaluated. According to Nyberg et al. (1998), a negative scan following a positive biochemical serum screen reduces the risk of Down syndrome by approximately 60%. A more recent study determined the likelihood of fetal trisomy 21 was reduced by 83-89% following a normal genetic sonogram (Vintzileos et al., 2002). Yeo and Vintzileos (2003) adjusted the risk for fetal trisomy 21 based on their own center's accuracy. The patient's a priori risk was multiplied by various likelihood ratios depending on the

presence or absence of specific ultrasound findings. For example, a patient beginning with a maternal age risk of 1:274 with a normal genetic sonogram has an adjusted risk for fetal trisomy 21 of 1:1370 (1:274 multiplied by 0.20) due to at least an 80% reduction in risk. Each center uses its own likelihood ratios and is still limited by operator error.

Attempts have been made to integrate the information from sonography into clinically useful risk assessment models for Down syndrome. Benacerraf and colleagues created a genetic sonogram scoring index for this purpose. In 1992, the scoring index proposed optimized the detection rate of Down syndrome among fetuses in mothers of any age. Each fetus was assessed for the presence of a nuchal fold greater than or equal to 6 mm, shortened femur and/or humerus, and pyelectasis. Structural malformations evaluated in the study included ventriculomegaly, heart defects, and limb abnormalities. The original scoring algorithm assigned major anomalies and thickened nuchal fold a value of 2 and all other soft markers were scored as a value of 1. Using a score of greater than or equal to 2 as a positive test, the results yielded an 81% detection rate and 4.4% false-positive rate (Benacerraf, Neuberg, Bromley, & Frigoletto, 1992).

Bromley and colleagues modified the scoring index by incorporating maternal age as a risk factor and also incorporated additional soft markers: echogenic intracardiac focus and hyperechoic bowel. Maternal age was divided into 3 categories, < 35 years, 35 to 39 years, and ≥ 40 years; each group with a corresponding score of 0, 1, and 2 respectively. The soft markers were assigned a value of 1. The study concluded that women < 35 years old received a positive score solely based on ultrasound markers. Patients between 35 and 39 years of age contributed a score of 1 based on age alone and only needed one additional ultrasound finding to receive a positive test. Finally, all women ≥ 40 years old automatically

scored positive based on age alone. Using the modified algorithm with maternal age, sensitivity for Down syndrome was 86.8% but a false positive rate of 27.1 % was reported (Bromley et al., 1997).

In an effort to create a more accurate algorithm, Bahado-Singh and colleagues introduced a technique to modify the previous dichotomous variables of "normal" and "abnormal" to a continuous mathematical variable for the biometric marker information. Their method involved standardizing the ultrasound measurements (i.e. nuchal thickness and humerus length) to minimize errors due to gestational age calculations. Using the same concept as serum marker value conversions, the standardized values were changed to multiples of the medians to allow the development of Gaussian distribution curves for the measurements in both Down syndrome and normal mid-trimester fetal groups (Bahado-Singh, Deren, Oz et al., 1998). This technique further individualized the risk of Down syndrome for a woman based on maternal age, biometric parameters, and serum markers. Using independent predictors of Down syndrome, Bahado-Singh and collaborators (2000) further evaluated their algorithm among a high-risk group of women consisting of 46 Down syndrome and 2,391 unaffected cases. Using maternal age, nuchal thickness, humerus length, serum AFP and hCG, researchers reported a sensitivity of 80.4% and 10% false-positive rate for Down syndrome.

In contrast to ultrasound screening in high-risk populations, the benefits of routine ultrasound screening in the general population have not been appropriately determined. According to Bahado-Singh et al. (2005), "There is a near complete absence of appropriately designed, prospective population-based ultrasound studies" (Bahado-Singh et al., 2005). Among the few studies, Shirley et al. (1992) used a hospital based population in the United

Kingdom for a mid-trimester ultrasound screening program. Six thousand one hundred eighty-three cases between 1989 and 1990 underwent routine ultrasound at an average of 19 weeks gestation. There were 10 confirmed cases of Down syndrome, of which 3 (30%) had an abnormal ultrasound before 22 weeks gestation. Six had no detectable anatomical malformations. The remaining case appeared normal at the 19 week scan but was diagnosed by karyotype during the third trimester secondary to fetal hydrops. The exam included evaluation of gross defects, nuchal skin thickness, renal pelvis, and ventriculomegaly. Jorgensen et al. (1999) performed a multi-center Scandinavian second-trimester ultrasound screening study of 27,844 low-risk women between the ages of 18 and 34 years. The group was evaluated for gross defects, femur length shortening and nuchal thickness. Among 32 cases of Down syndrome, 6.3% were detected by ultrasound. A retrospective study by Howe et al. (2000) reviewed 31,259 pregnancies in a maternity unit in the UK between 1993 and 1998. The overall detection rate of Down syndrome by routine ultrasonography was 68%. The detection rate among women less than 35 years of age was 53% (9/17). The study did not clearly define thresholds used for detection. A similar study of 36,410 women of average age 27 years underwent mid-trimester serum screen and ultrasound between 18 and 22 weeks. Among 24,276 screen-negative cases, twenty percent (2/10) Down syndrome fetuses had sonographic abnormalities. Nine thousand nine hundred and sixty study participants declined serum screening; sonographic abnormalities were detected in 4/7 (57%) of fetuses with Down syndrome. The detection of Down syndrome increased by 11% when mid-trimester ultrasounds were compared to serum AFP and hCG screening alone. The study included several soft markers including pyelectasis, bowel echogenicity, shortened long bones, ventriculomegaly, nuchal thickness, and choroid plexus cysts

(Roberts, Walkinshaw, McCormack, & Ellis, 2000). Finally, Stoll and colleagues reviewed routine mid-trimester ultrasound screening on 119,099 consecutive pregnancies among low-risk French women. Only ten of fifty-four (18.5%) Down syndrome fetuses were identified by an abnormal ultrasound exam. The overall sensitivity for detecting Down syndrome by ultrasound was 8.1% (10/123). This study only evaluated gross anatomical defects and specificity was reported as 100% (Stoll, Dott, Alembik, & Roth, 1993). In general, low-risk population studies reveal that mid-trimester ultrasound screening has decreased sensitivity for Down syndrome detection.

Patient Perceptions

Regardless of the published detection rate of Down syndrome by ultrasound, individual perceptions of this number appear to be a factor women consider when deciding whether or not to undergo an invasive diagnostic test. In conjunction with the perceived detection rate of Down syndrome, each woman has her own background knowledge of ultrasound and its sensitivity and purpose. Previous studies vary in their findings making it difficult to apply general recommendations to our patient population. To our knowledge, no studies have been performed on a United States population. Previous studies performed have been primarily on unselected populations of pregnant women examining women's attitudes, knowledge, and perception of routine sonograms (Chan et al., 2008; Georgsson Ohman & Waldenstrom, 2008; Hyde, 1986; Lalor & Devane, 2007). Chan et al. (2008) explored the background knowledge, expectations and experiences of a Chinese population of pregnant women regarding routine second trimester ultrasound. The study reported an overall positive experience from the event but an unsatisfactory knowledge of the

ultrasound. A Swedish based populations study including women of all risk reported pregnant women had high expectations of the routine second trimester ultrasound, and their strongest motivation for the exam was to determine the health of the baby (Georgsson Ohman & Waldenstrom, 2008). Smith et al. (2004) and Basama, Leonard, & Leighton (2004) reported a poor patient knowledge of the 20 week anomaly scan performed on pregnant women in the United Kingdom. Both studies concluded that patients need to better informed and more educational efforts should be made. In general, studies have shown that women's expectations exceed ultrasound capabilities (Chan et al., 2008; Lalor & Devane, 2007; Smith, Titmarsh, & Overton, 2004).

Some reports have shown sufficient understanding and an accurate perception of the prenatal ultrasound, particularly among populations that are provided written information about the ultrasound prior to the appointment. Smith et al. (2004) created an education program and compared two populations' knowledge about the 20 week anomaly scan. The found patients who received information prior to the exam answered knowledge-based questions correctly more often than the control group. Larsen and collaborators included women of all risk and explored their background knowledge of ultrasound screening in the second trimester and their overall experience. They asked a series of open and close ended questions which revealed the following themes. Women have a relatively accurate understanding of ultrasound examinations supplied by family and friends; however, the background knowledge can be increased by improved quality and access to information. Their primary goal is to maintain the health of their baby (Larsen Nguyen, Munk, Svendsen, & Teisner, 2000). In general, each study population differs slightly in their background knowledge of prenatal ultrasounds, but there is a common trend of under-estimating

limitations and over-estimating the capabilities of the ultrasound examination. This is evident by the multitude of studies reporting a strong reassurance of the health of the baby from a normal ultrasound and high expectations of the ultrasound to detect any anomalies or problems.

Different approaches have been taken to determine current perceptions of ultrasound, both routine exams and anatomy scans. One Swedish study evaluated the perception of information given before and during routine ultrasound examinations. As part of the evaluation, women were questioned about the purpose of second trimester ultrasound scan. Although the information provided prior to ultrasound scanning explicitly stated the main purposes of the scan to be dating and detection of multiple gestation, 89% of women and 84% of men believed the purpose of the ultrasound was to detect fetal abnormalities. This reflects that the primary parental concern is the health of the baby (Eurenius, Axelsson, Gallstedt-Fransson, & Sjoden, 1997).

Basama and colleagues surveyed their patient population including women of all risk in the UK to assess perception of the purpose of the anatomy scan. The hospital provided leaflets containing information regarding the 20 week anomaly scan prior to the patient's appointment. The group assessed the adequacy of the information provided to the patient. Ninety-five percent of the women surveyed considered the purpose of the anomaly scan to be evaluation for structural abnormalities, demonstrating a good understanding. However, 32% believed the purpose of the exam was to detect chromosomal abnormalities, and 32% of women thought the scan would identify Down syndrome. Women expected the ultrasound to identify 76%, 76%, 33% and 90% of kidney, limb, heart, and spinal abnormalities, respectively. Ninety-two percent of women had never heard of soft markers

for chromosome abnormalities. Although women had a good understanding of the purpose of the ultrasound, the group concluded that only 8% of women had a realistic assessment of the capability of the anomaly scan (Basama, Leonard, & Leighton, 2004).

One study in the UK determined patients' knowledge of the 20-week fetal anatomy scan and found women were more informed after receiving a patient information sheet regarding the purpose of ultrasound (Smith et al., 2004). A Canadian study used a questionnaire to evaluate the understanding of ultrasound in a low-risk population of women attending a second-trimester anatomy scan. Fifty-five percent of women stated they had not received previous information about ultrasound scanning prior to the exam, and 46% did not believe the ultrasound would be used as a screening tool for anomalies. These results highlight the need for proper evaluation of women's understanding of sonography as a screening method for fetal abnormalities in order to meet requirements for informed choice (Kohut, Dewey, & Love, 2002). The authors of the above mentioned studies highlight the lack of information provided to patients regarding the ultrasound and discuss the issue of informed consent.

Even when provided information before and/or after ultrasound examination, patients have previously established expectations and knowledge of the procedure that are important to understand in order to provide appropriate counseling and obtain informed consent.

Significance

Current literature assessing patient perceptions and knowledge of ultrasound is inconsistent. Results range from appropriate to poor understanding, and conclusions lack

consistent general recommendations. Study populations and designs are also diverse making it difficult to apply the information reported to the general population. There are no perception studies performed on a United States based population. In addition, no studies concentrate on perceptions of targeted ultrasound and detection rates of Down syndrome in high risk populations. Many women who test positive on second trimester maternal serum screening are referred for genetic counseling. Therefore, this information is very important for providers of genetic counseling to improve patient education and obtain informed consent. Genetic counselors support patients and help them understand maternal serum screen results as well as the risks, benefits and limitations of additional screening, such as ultrasound, and diagnostic tests. Targeted ultrasound is a screening tool widely available during pregnancy; however, the diagnostic capabilities of ultrasound technology continue to develop over time. Patient's knowledge and understanding of available screens continues to change. Thus, it is important to continuously evaluate current understanding for proper counseling.

Study Aims

The aim of this study is to determine the perception and knowledge of targeted ultrasound in women who screen positive for Down syndrome in the first or second trimester, and to assess the perceived detection rate of Down syndrome by targeted ultrasound in this population. With this information, genetic counselors and associated health care professionals may be better equipped to address the screening capabilities of ultrasound and provide accurate information for informed consent.

MATERIALS AND METHODS

Study Design

The aim of this study was to determine perception and knowledge of targeted ultrasound in women who screen positive for Down syndrome in the first or second trimester, and to assess the perceived detection rate of Down syndrome by targeted ultrasound in this population. A self-administered questionnaire (Appendix A) was used to determine participants' level of understanding of ultrasound and its role in detecting Down syndrome. Demographic information obtained from the survey included ethnicity, education, income, and pregnancy history.

Hypothesis

Women who screen positive for Down syndrome do not have an accurate perception of the detection rate for Down syndrome by targeted ultrasound, as well as the general capabilities of targeted ultrasound.

Study Approval

The Committee for the Protection of Human Subjects of the University of Texas-Houston Health Science Center approved this study on June 16, 2010.

Study Population

The study population consisted of all English and Spanish speaking pregnant women who were referred to the University of Texas Maternal-Fetal Medicine clinics, which

includes Memorial Hermann Professional Building, St. Joseph Medical Center, Memorial Hermann Hospitals – Katy, Memorial City, Sugar Land, Southeast, and Southwest, for positive first trimester or second trimester screens for Down syndrome. Multiple sites were included to obtain the greatest number of participants given the time frame for collection. Patients had to be at least 18 years of age to participate. All women of advanced maternal age (≥ 35 years of age) were excluded.

Sample Size

The anticipated sample size was 75 women. The sample size was based upon number of patients that met the above criteria that attended clinic in the previous months as recorded in the clinical database and the number of months estimated for recruitment. There was no maximum number at which we stopped recruiting for the study.

Questionnaire

A descriptive questionnaire was created in order to access a sample of women attending a high risk clinic for a targeted (level II) ultrasound. A review of the literature did not identify a questionnaire specifically evaluating women's perceptions of a targeted ultrasound and its role. Therefore, an instrument was created and revised through several phases by the committee members to determine whether it was clearly worded and appropriately structured to gather desired information. A similar review process was conducted by Kohut, Dewey, and Love (Kohut et al., 2002) when developing a questionnaire for their prenatal patients aimed to determine women's perceived value of the information received by ultrasound and principles of informed consent. Experts within the

fields relevant to the questionnaire reviewed the screening tool to assess content and validity.

The questionnaire was constructed on the premise of similar studies in China and Denmark (Chan et al., 2008; Larsen et al., 2000). There were three main sections: (1) pregnancy history and sociodemographic characteristics; (2) detection of Down syndrome by targeted ultrasound; and (3) knowledge of targeted ultrasound.

1. Pregnancy history and sociodemographic questions: There were nine questions regarding the patient's previous and current pregnancy history as well as common demographic questions (average household income, education level, and race/ethnicity).
2. Detection of Down syndrome by targeted ultrasound questions: There were four questions in this section, used to determine the perception of the detection rate of Down syndrome by ultrasound.
3. Knowledge of targeted ultrasound questions: There were two questions used to determine if a patient knew what a targeted ultrasound was and if they had previously had one performed. The final question had a subset of fifteen items. The goal of this question was to determine if the participant believed it is possible for a targeted ultrasound to identify any one of the listed items.

Every question was multiple choice. At the midpoint of collection, a modification was made to the questionnaire to include "Don't know" as an answer choice for two of the questions pertaining to the detection rate of Down syndrome by targeted ultrasound. This was done due to the high non-response rate for the two questions.

Data Collection

Women meeting study criteria were identified prior to their genetic counseling appointment. An information sheet describing the study was given to eligible patients (Appendix B). Women who chose to participate completed the questionnaire and returned them to the genetic counselor or front desk staff. Data collection began on June 21, 2010 and ended on February 4, 2011.

Statistical Analysis

Data collected from the questionnaires was entered into a Microsoft Access database. The database was analyzed using statistical analysis software program, STATA (v.10, College Station, TX). For our primary analysis, we performed a descriptive analysis to evaluate the perception/knowledge of the detection of Down syndrome by targeted ultrasound. The number and proportion of women selecting each answer option in questions 9-11 were tabulated, along with the median and most common response for each question. A similar descriptive analysis of each defect in question 12, provided information on perception/knowledge of detection of specific congenital defects. A secondary analysis of the data was performed after stratifying by various demographic factors (race/ethnicity, household income), pregnancy history and history of birth defects. For the stratified analysis we used contingency tests (Fisher's exact test, Chi-squared test) to compare the proportion of women that selected each answer option. External validity for demographic information obtained by the questionnaire was confirmed by checking with previous studies performed on the same clinic population. Results with a p-value of less than 0.05 were considered

statistically significant. The null hypothesis used for all statistical tests was that there was no difference between groups.

RESULTS

Between June 21, 2010 and February 4, 2011, 77 women chose to participate in the study. Of the 77 participants, the majority were recruited from UTPB (32%) and St. Joseph Medical Center (26%). The other Memorial Hermann collection sites, Memorial City, Katy, Southwest, Southeast, and Sugar Land had 8%, 13%, 4%, 9%, and 8% of collected surveys respectively. Nearly 94% of the surveys collected were in English.

Demographics

The racial-ethnic background of the participants was divided among five categories: Caucasian, African American, Hispanic, Asian, and other. Two individuals chose "other" and identified themselves as Asian Indian and Middle Eastern. These individuals were grouped into the Asian category for statistical analysis. Table 1 shows the racial-ethnic breakdowns for each group.

The highest level of education completed was categorized by some high school, high school, some college, bachelor degree, and post-graduate or professional degree. To increase the power in the analysis, the education levels were re-grouped from five groups into two groups: less than a college degree and a college degree or higher (Table 1). The combined household income categories were also tabulated (Table 1).

Table 1: Demographic Background of Participants

	Demographics	Counts (n)	Percent (%)
Race/Ethnicity*			
	Caucasian	29	39.19
	African American	16	21.62
	Hispanic	20	27.03
	Asian	9	12.16
	Total	74	100
Education**			
	Less than College Degree	51	69.86
	College Degree or Higher	22	30.14
	Total	73	100
Income***			
	< $10,000	14	20
	$10,000-$25,000	13	18.57
	$25,000-$50,000	17	24.29
	$50,000-$75,000	13	18.57
	$75,000-$100,000	5	7.14
	> $100,000	8	11.43
	Total	70	100
* 3 individuals did not answer this question			
** 4 individuals did not answer this question			
*** 7 individuals did not answer this question			

Correlations between race/ethnicity, education and income were evaluated and significant differences were found between the results from race/ethnicity and education ($p<0.001$), race/ethnicity and income ($p=0.001$), and education and income ($p<0.001$). In general, individuals with more education were more likely to have a higher gross annual income. Asians and Caucasians were more likely to have completed higher education than African Americans and Hispanics (Table 2). More specifically, there was a significant difference between the education levels of Hispanics and Caucasians ($p=0.004$) and Hispanics and Asians ($p<0.001$).

Table 2: Distribution of Total Household Income by Racial-Ethnic Background

	Racial-Ethnic Background				
Income	African American	Hispanic	Asian	Caucasian	Total
Less than $10,000	5	5	1	3	14
$10,000-$25,000	3	5	0	5	13
$25,000-$50,000	3	6	2	6	17
$50,000-$75,000	2	3	2	6	13
$75,000-$100,000	1	0	1	3	5
Greater than $100,000	0	0	3	5	8
Total	14	19	9	28	70

Finally, there was a significant difference between the racial distribution among the collection sites (p=0.009). St. Joseph Medical Center was more strongly represented by Hispanics and UTPB and Memorial Hermann Katy had a higher percentage of Caucasians. The other clinics had a slightly more diverse population with regard to race/ethnicity.

Pregnancy History

Participants reported total number of pregnancies, number of living children, and number of ultrasounds during current pregnancy (Table 3).

Table 3: Pregnancy History of Participants

Pregnancy History		
	Number	n (%)
Total Pregnancies		
	1	30 (38.96)
	2	16 (20.78)
	3	16 (20.78)
	4	10 (12.99)
	5 or more	5 (6.49)
Living Children		
	0	34 (44.16)
	1	20 (25.97)
	2	15 (19.48)
	3	7 (9.09)
	4	1 (1.3)
Ultrasound During Pregnancy*		
	No	7 (9.09)
	Yes	68 (88.31)
Number of Ultrasounds**		
	1	31 (40.26)
	2	20 (25.97)
	3	8 (10.39)
	4	6 (7.79)
	5	0 (0)
	6	1 (1.3)
* 2 individuals did not answer this question		
** 11 individuals did not answer this question		

Information regarding women's experience with a genetic disorder or birth defect was obtained. Women were asked if they had a child with a genetic condition and/or birth defect, and 96.1% (74/77) answered no. Of the three women who reported yes, the conditions or birth defects recorded were "Thalassemia B", "tumor on head", and "sacral dimple hemangioma." Women were also asked if they knew anyone with a genetic condition

or birth defect. Almost 29% (22/77) answered yes. Figure 1 and Table 4 show the breakdown of answers for this question.

Figure 1: Do You Know Anyone with a Genetic Disorder or Birth Defect?

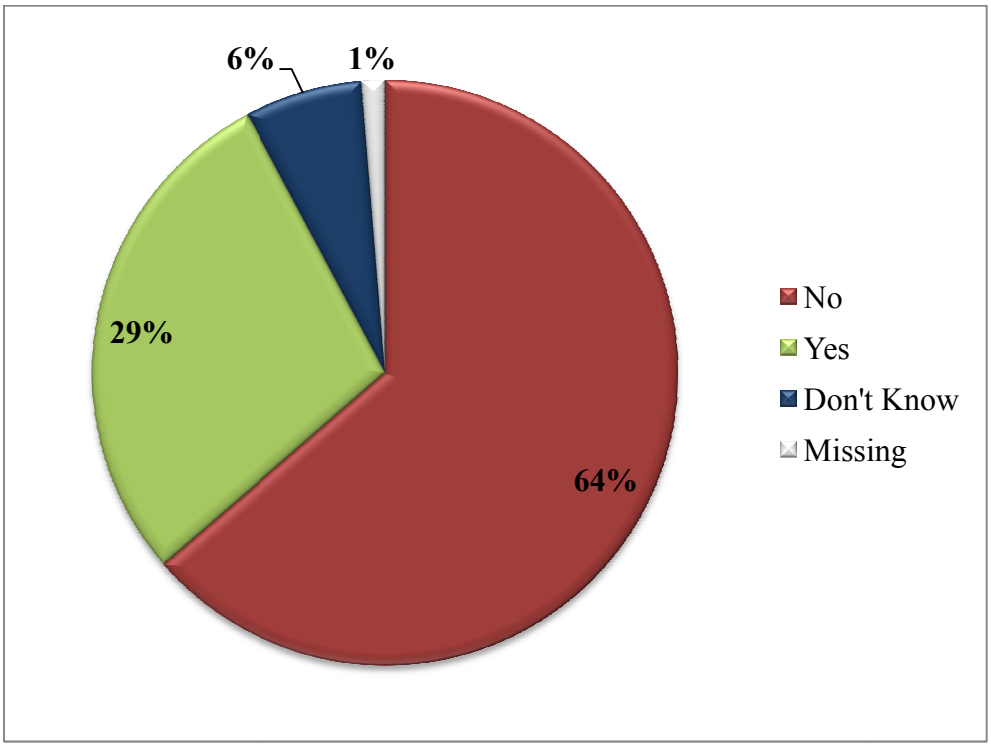


Table 4: If yes, what condition/birth defect did they have?*

Genetic Condition or Birth Defect	Frequency
Spina bifida	1
Down syndrome	11
Cleft lip and palate	1
Autism	1
Tuberous sclerosis	1
Trach-ear deformity	1
Hand/leg deformity	1
Trisomy 13	1
Infertility	1
Unknown	1

*Data not mutually exclusive and 5 women did not answer

Knowledge of Targeted Ultrasound

Several questions were designed to evaluate the participants' knowledge of targeted ultrasound. A number of the women omitted responses to some of the questionnaire items, so the number of respondents varied per question. Question two (Q2) categorized women into groups: women who heard of a targeted ultrasound, women who have not heard of a targeted ultrasound, and women who did not know if they had heard of a targeted ultrasound. Fifty-five (73%) women had heard of a targeted ultrasound (Figure 2a). Of the women who reported hearing of a targeted ultrasound, question 2a (Q2a) asked what was the source of their information (Figure 2b). Question 3 (Q3) asked how many targeted ultrasounds have you had prior to today in any pregnancy (current or past). Most women reported never having a targeted ultrasound (63/77) regardless of whether they had heard of one or not. Three women who reported never hearing of a targeted ultrasound recorded having 1, 3, and 4 targeted ultrasounds. Figure 3 shows the overall number of targeted ultrasounds reported by participants.

Figure 2a: Q2: Have you heard of a targeted ultrasound?

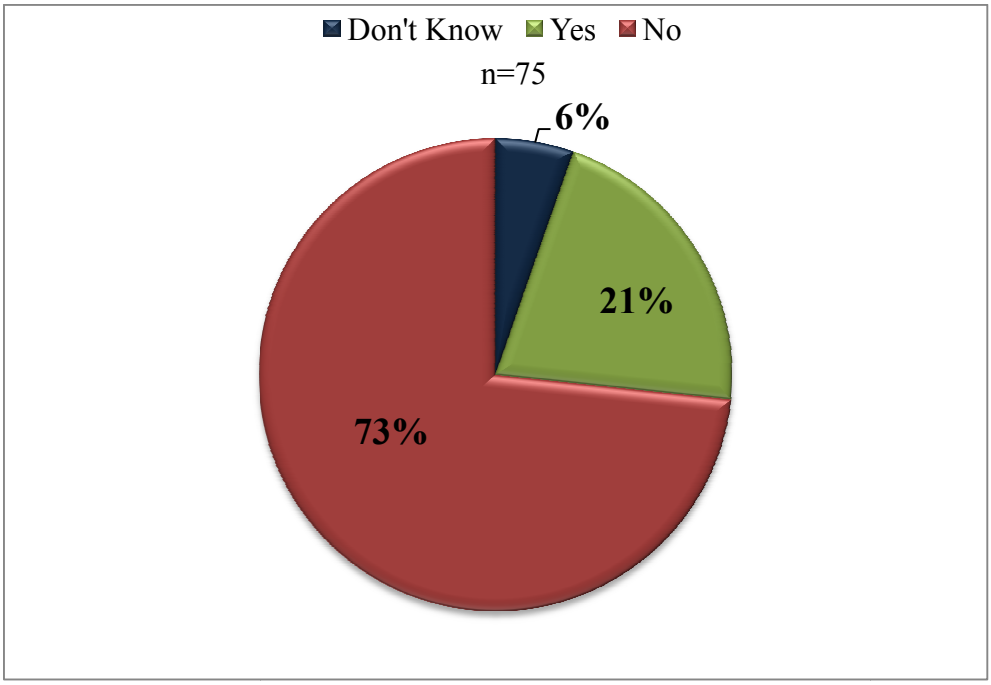
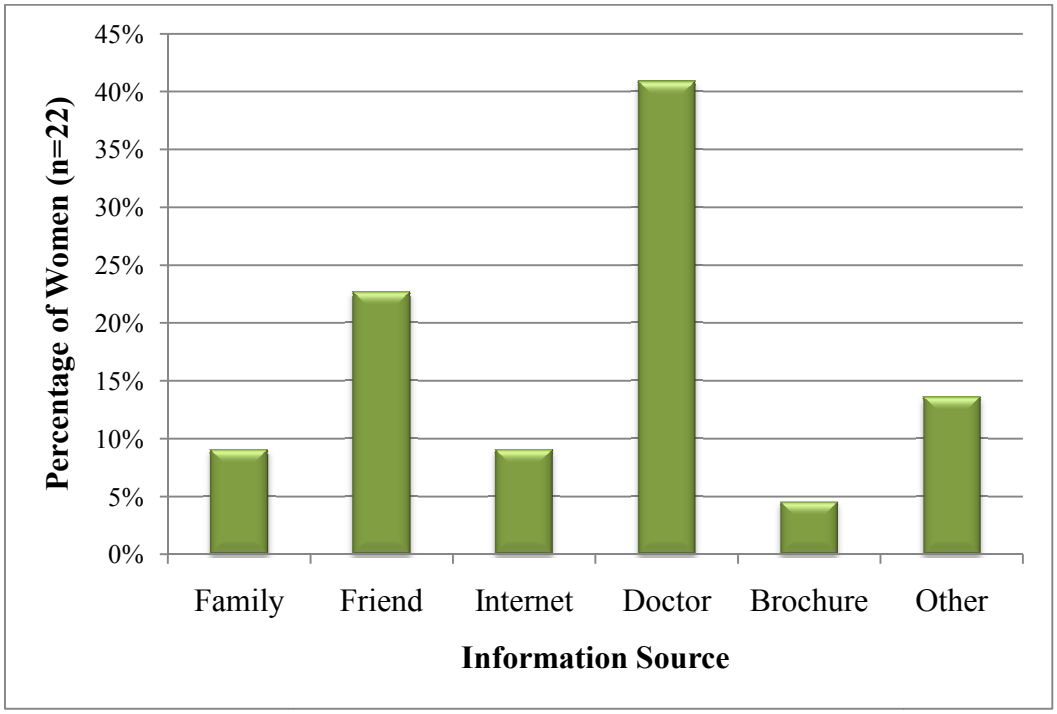
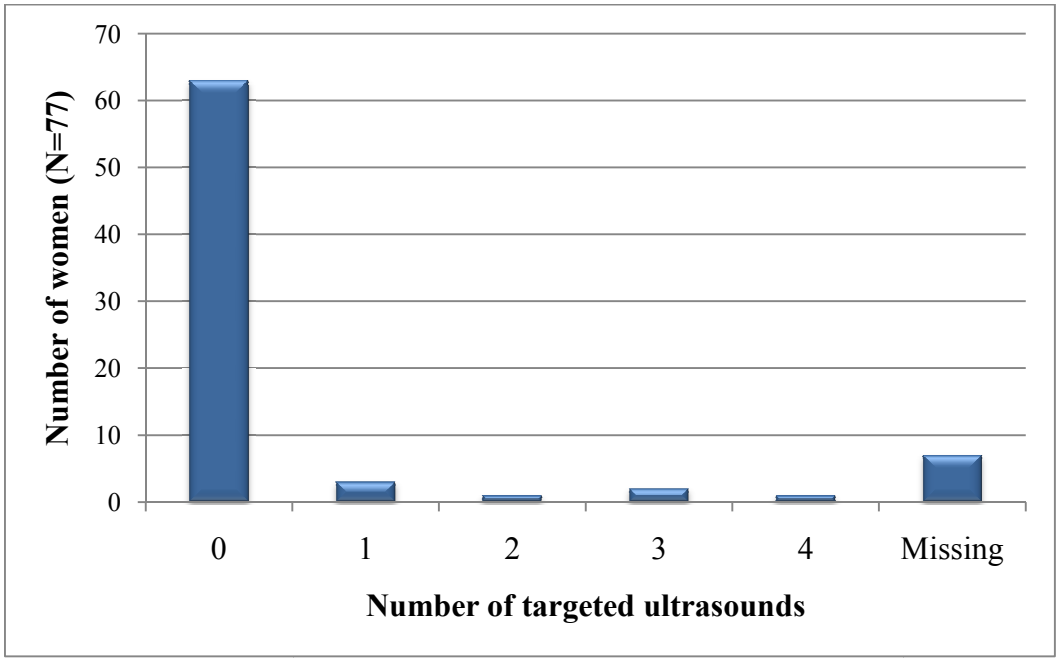


Figure 2b: Q2a: If yes, where did you hear about the targeted ultrasound?*



*Data not mutually exclusive

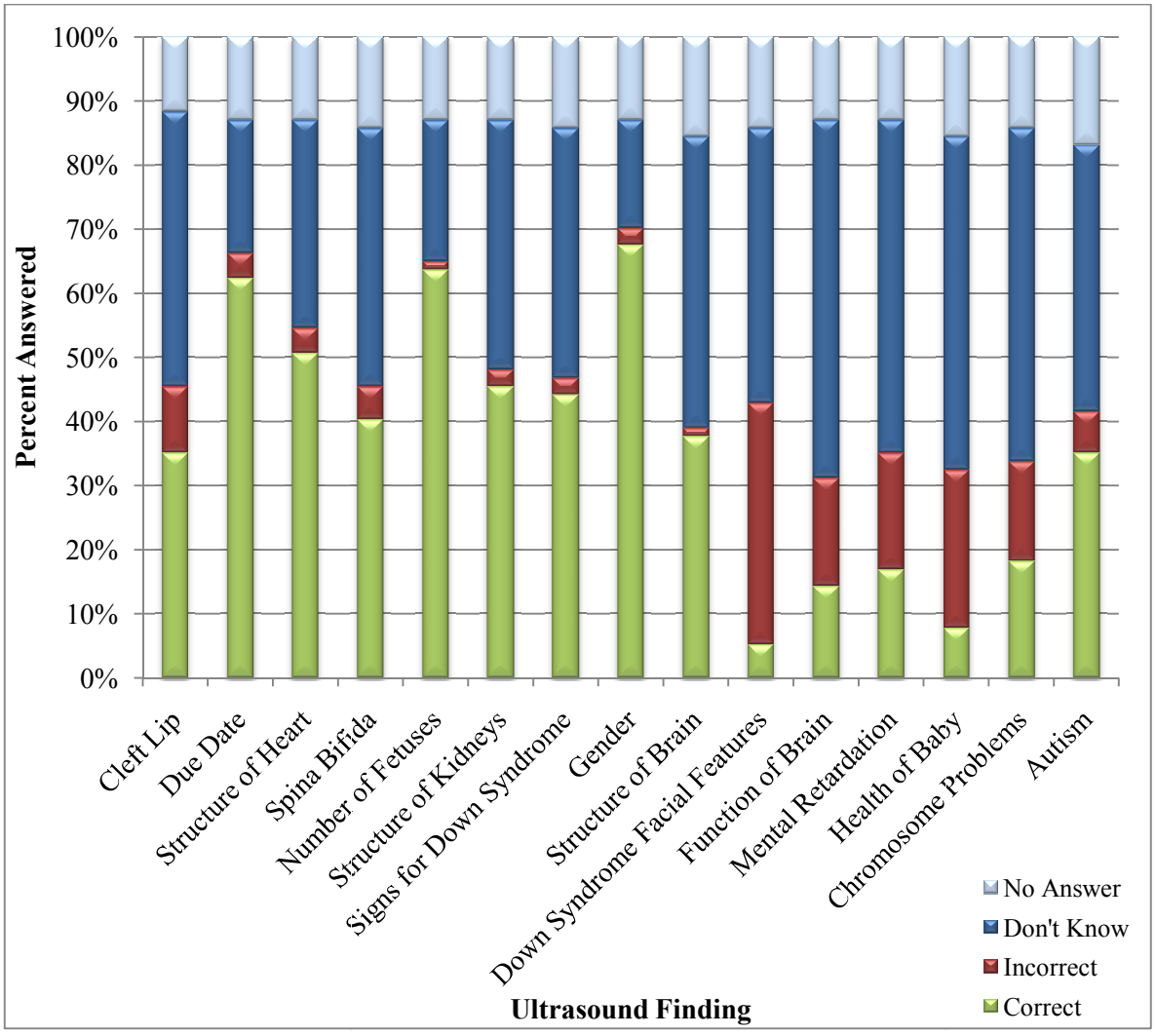
Figure 3: Q3: How many targeted ultrasound have you had prior to today in any pregnancy (current or past)?



Question number 12 asked: With the understanding that ultrasound may be limited by gestational age and position of baby, in most cases, it is possible for a targeted ultrasound to detect any of the following in the baby: cleft lip, function of baby's brain, due date, structure of heart, spina bifida, mental retardation, number of babies (single v. twin), health of baby, chromosome problem(s), facial features of Down syndrome, kidney structure, signs of Down syndrome, gender of baby, autism, and structure of brain. Choices for the answer included "yes," "no," and "don't know." Answers to each question were categorized by correctness. For example, it is possible for a targeted ultrasound to detect cleft lip, so the correct answer is yes. Conversely, it is not possible for a targeted ultrasound to detect mental retardation, so the correct answer is no. In this case, individuals that chose "yes" as their answer for detection of cleft lip and individuals that answered "no" for detection of

mental retardation were labeled as correct. This categorization was done for each question. Figure 4 shows the percentage of each question that was answered correctly, incorrectly, don't know, and unanswered. When comparing answers about ultrasound findings that refer to structural features (e.g. cleft lip, due date, and gender) to those that refer to functional or biological features (e.g. health of baby, mental retardation, and autism), women answered the structural questions correctly more often. For each ultrasound finding, 9 to 13 (11-17%) women did not answer the question.

Figure 4: Is it Possible for a Targeted Ultrasound to Detect Each of the Following in the Baby?



Fisher exact tests were performed to determine if the answers for ultrasound knowledge questions differed by race/ethnicity (Table 5). Missing data was not included in the analysis in order to avoid skewed results. Responses to ultrasound knowledge questions were significantly different by race/ethnicity for the following: due date, number of fetuses, chromosome problem(s), and kidney structure with p values <0.05.

Table 5: Fisher Exact Tests for Significance between Ultrasound Knowledge and Race/Ethnicity

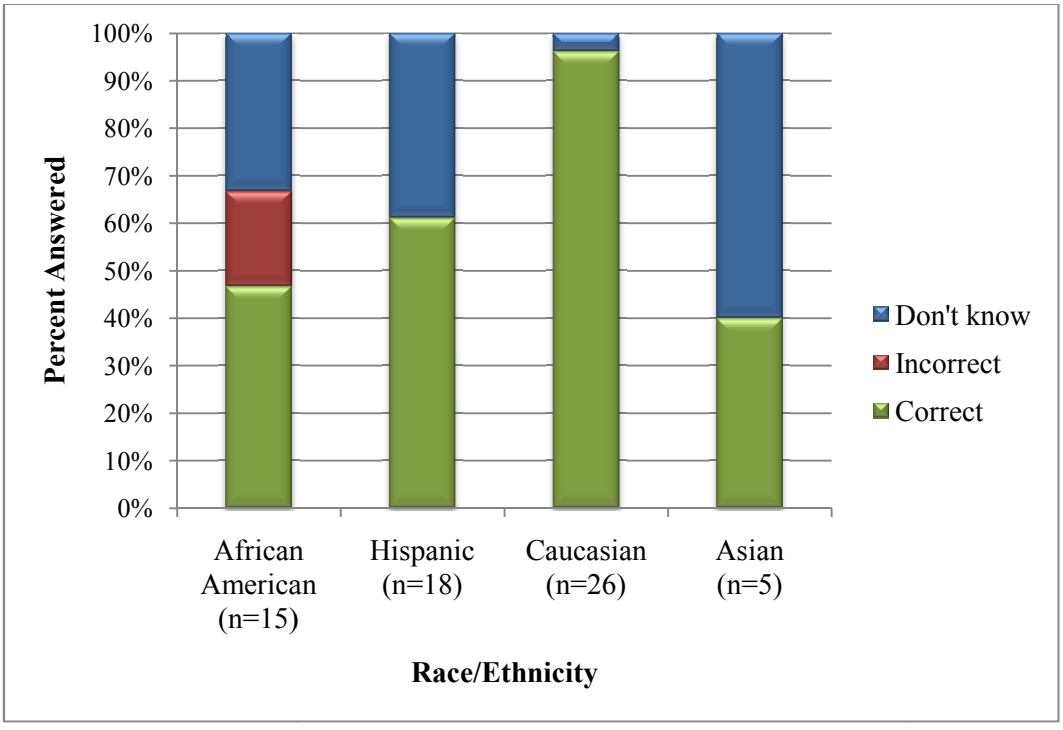
Ultrasound Finding	p=value*
Cleft lip	0.140
Function of baby's brain	0.182
Due date	**0.001**
Structure of heart	0.199
Spina bifida	0.589
Mental retardation	0.120
Number of babies	**0.022**
Health of baby	0.543
Chromosome problem(s)	**0.015**
Facial features of Down syndrome	0.278
Kidney structure	**0.009**
Signs of Down syndrome	0.113
Gender of baby	0.057
Autism	0.355
Structure of brain	0.141

***p<0.05 is significant**

Caucasians correctly answered ultrasound's ability to determine due date more frequently than African Americans, Hispanics, and Asians (Figure 5). Caucasians chose the correct answer more frequently than Hispanics when responding to ultrasound's ability to detect

number of fetuses (Figure 6). When answering whether ultrasound is able to detect chromosome problem(s), the majority of individuals, regardless of race/ethnicity, did not know the correct answer. However, Hispanics were significantly different than the other racial groups in that none answered the question correctly and the majority chose "don't know" as their answer (Figure 7). Lastly, Caucasians were more likely to choose the correct answer for ultrasound's ability to determine kidney structure compared to Hispanics and Asians (Figure 8).

Figure 5: Answers to Targeted Ultrasound's Ability to Determine Due Date by Race/Ethnicity

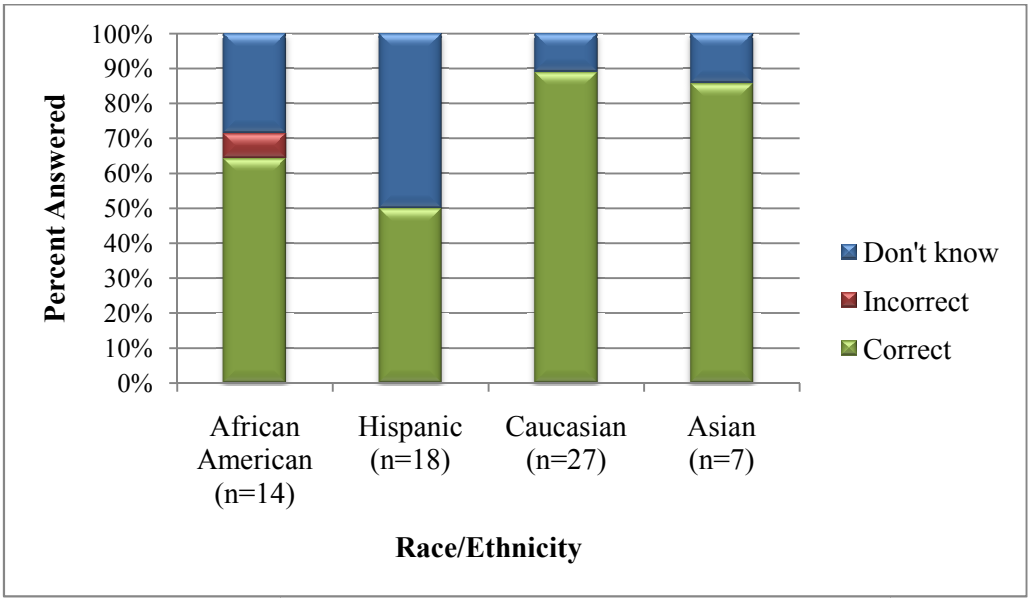


(a) Significant difference between African American and Caucasian ($p<0.001$)

(b) Significant difference between Hispanic and Caucasian ($p=0.005$)

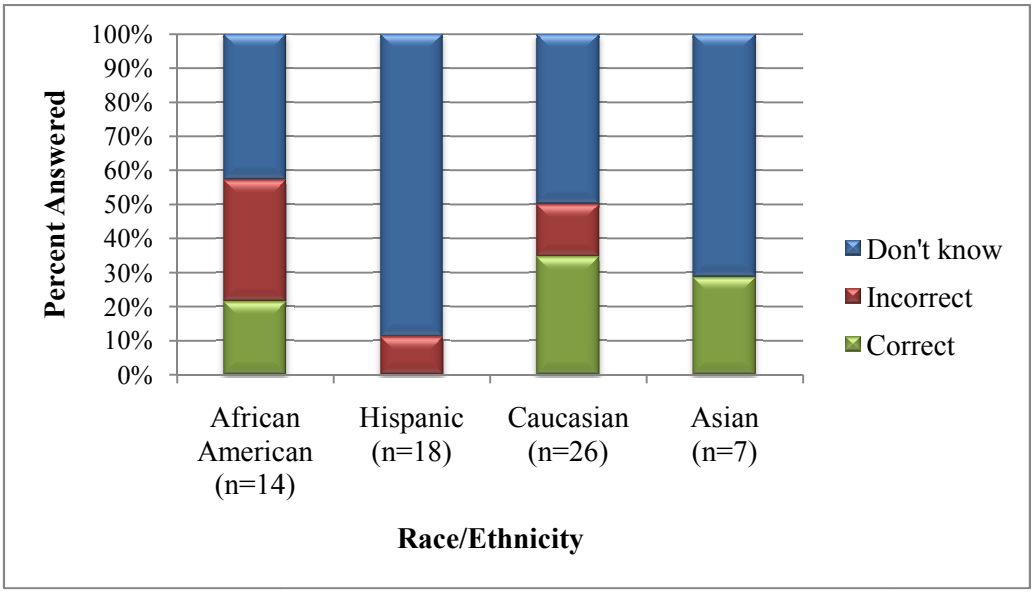
(c) Significant difference between Asian and Caucasian ($p=0.008$)

Figure 6: Answers to Targeted Ultrasound's Ability to Identify Number of Fetuses by Race/Ethnicity



(a) Significant difference between Hispanic and Caucasian (p=0.006)

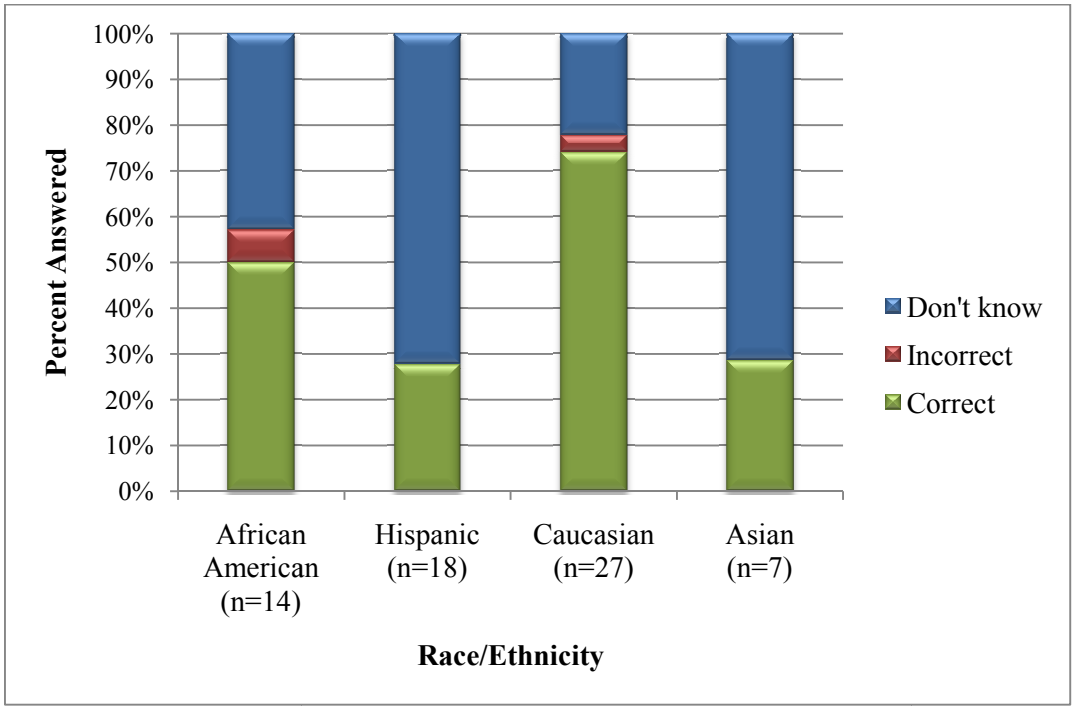
Figure 7: Answers to Targeted Ultrasound's Ability to Detect Chromosome Problem(s) by Race/Ethnicity



(a) Significant difference between Hispanic and Caucasian (p=0.008)

(b) Significant difference between African American and Hispanic (p=0.013)

Figure 8: Answers to Targeted Ultrasound's Ability to Determine Kidney Structure by Race/Ethnicity



(a) Significant difference between Hispanic and Caucasian (p=0.002)

(b) Significant difference between Asian and Caucasian (p=0.037)

Similarly, the answers for each ultrasound knowledge question were compared to education level of participants. Table 6 includes all Fisher exact test p values. Responses were significant for the following: cleft lip, function of baby's brain, and structure of brain.

Table 6: Fisher Exact Tests for Significance between Ultrasound Knowledge and Education

Ultrasound Finding	p=value*
Cleft lip	**0.046**
Function of baby's brain	**0.004**
Due date	0.697
Structure of heart	0.461
Spina bifida	0.739
Mental retardation	0.063
Number of babies	0.112
Health of baby	0.698
Chromosome problem(s)	0.448
Facial features of Down syndrome	0.144
Kidney structure	0.336
Signs of Down syndrome	0.088
Gender of baby	0.370
Autism	0.644
Structure of brain	**0.024**

***p<0.05 is significant**

A few general trends were observed. First, individuals in the higher education category were more likely to choose the correct answer. Second, individuals with less education were more likely to choose "don't know." Third, whether correct or incorrect, individuals that had a college degree or higher were more likely to choose an answer as opposed to "don't know" (Figures 9-11).

Figure 9: Answers to Targeted Ultrasound's Ability to Detect Cleft Lip by Education

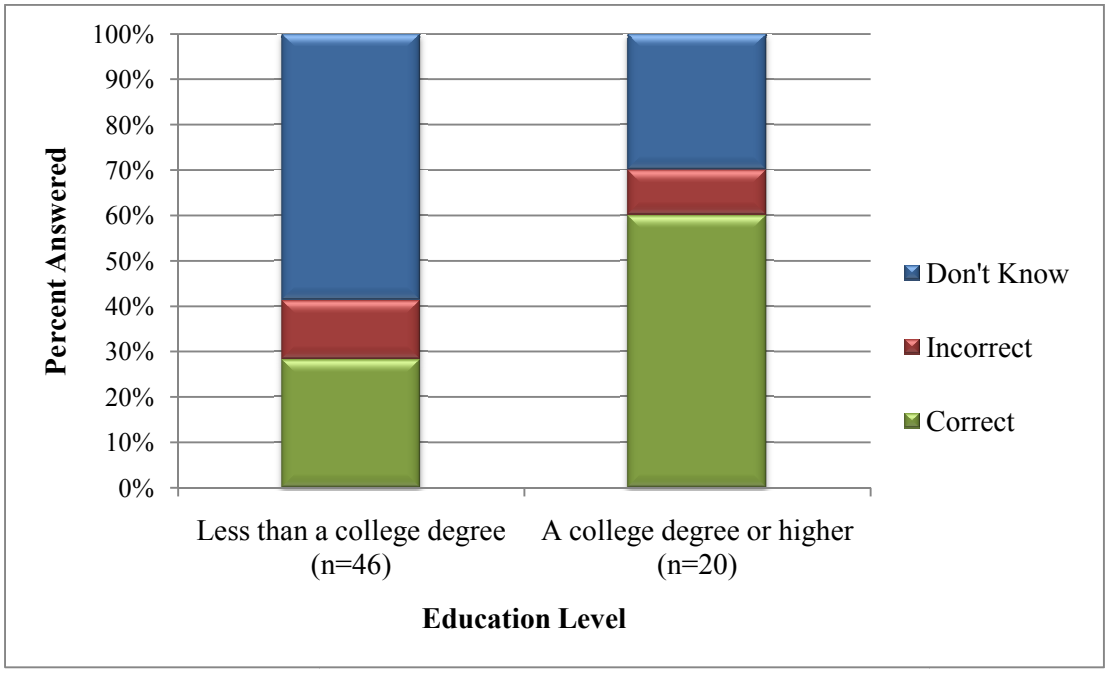


Figure 10: Answers to Targeted Ultrasound's Ability to Determine Function of Baby's Brain by Education

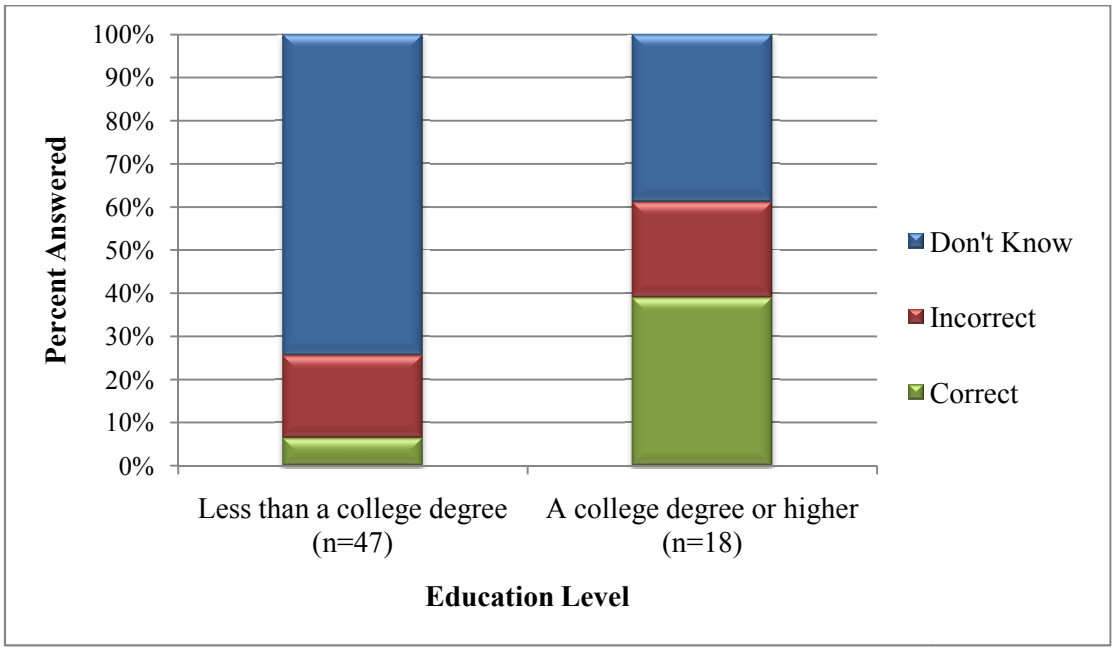
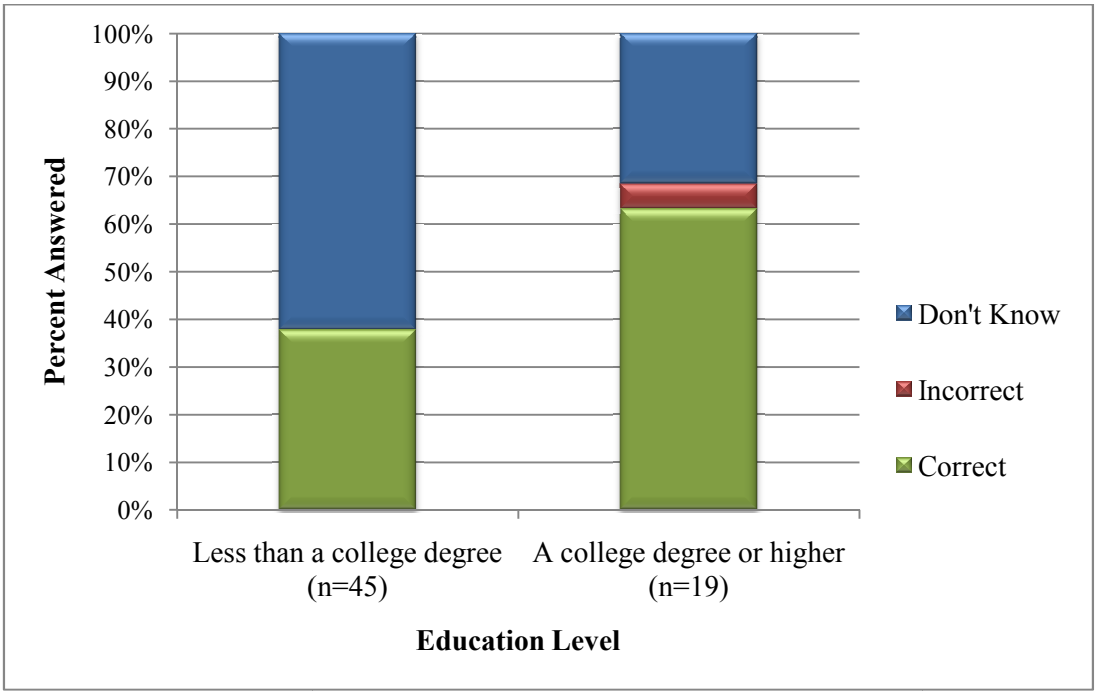


Figure 11: Answers to Targeted Ultrasound's Ability to Detect Structure of Brain by Education



To determine the more influential variable for participants' answers, responses were stratified by education and then tested for significance by race/ethnicity. Results were not significant for comparisons between race/ethnicity within the higher education category. Ultrasound findings including due date, chromosome problem(s), and kidney structure were significant between certain racial groups within the lower education category. Specifically, among individuals with less than a college degree, significant differences were seen between answers given by African Americans and Caucasians, as well as Hispanics and Caucasians. In both circumstances, Caucasians were more likely to answer correctly. Among participants with less than a college degree answering the ultrasound knowledge question regarding chromosome problem(s), Caucasians were more likely to answer correctly and Hispanic individuals primarily answered "don't know." Similarly, a significant difference

between responses from African Americans and Hispanics was due to the vast majority of Hispanics answering "don't know." The same trend was seen between Hispanic and Caucasian respondents for detection of kidney structure. Although a consistent trend was not observed, it appears race/ethnicity is an influential component among individuals that are less educated. Conversely, data was stratified by race/ethnicity and tested for significance by education. No trends were observed. In summary, it appears race/ethnicity is not confounding education, and education is only confounding race/ethnicity when individuals are less educated.

Finally, participants' responses were compared to whether or not women had heard of a targeted ultrasound. Answers choices for the question, "have you heard of a targeted ultrasound?" were "yes," "no," and "don't know." Responses were grouped into two categories: yes and no. Individuals that chose no or don't know as their response were grouped together for analysis in the no category. This was done to compare women that knew they had heard of a targeted ultrasound to others. Results are shown in Table 7.

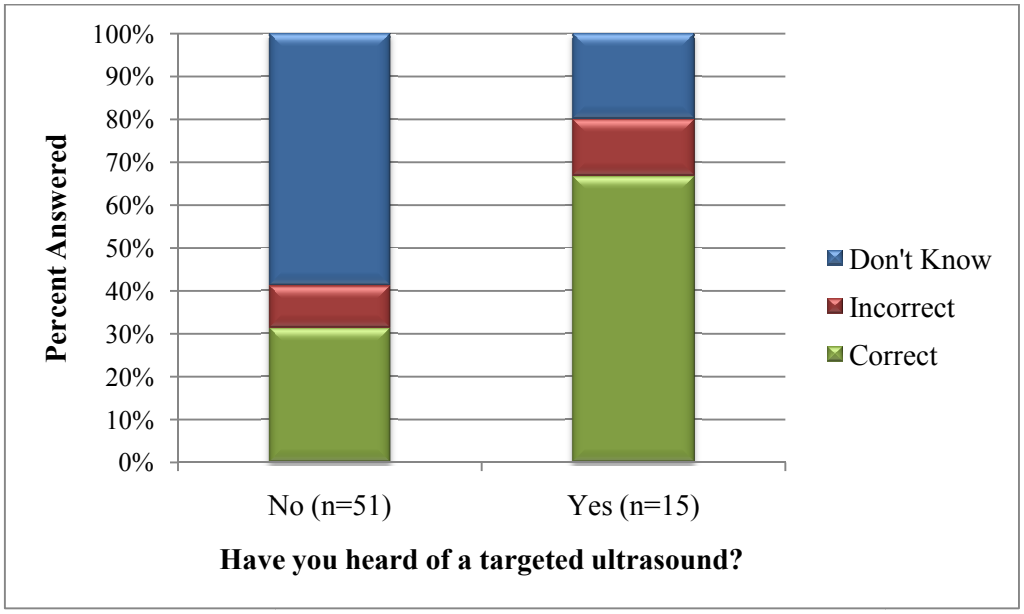
Table 7: Chi Squared Tests for Significance between Ultrasound Knowledge and Women Who Have Heard of a Targeted Ultrasound

Ultrasound Finding	p=value*
Cleft lip	**0.019**
Function of brain	0.110
Due date	0.756
Structure of heart	0.113
Spina bifida	0.086
Mental retardation	**0.035**
Number of babies	0.800
Health of baby	0.065
Chromosome problem(s)	**0.023**
Facial features of Down syndrome	0.073
Kidney structure	0.147
Signs of Down syndrome	0.075
Gender of baby	0.467
Autism	0.380
Structure of brain	0.503

***p<0.05 is significant**

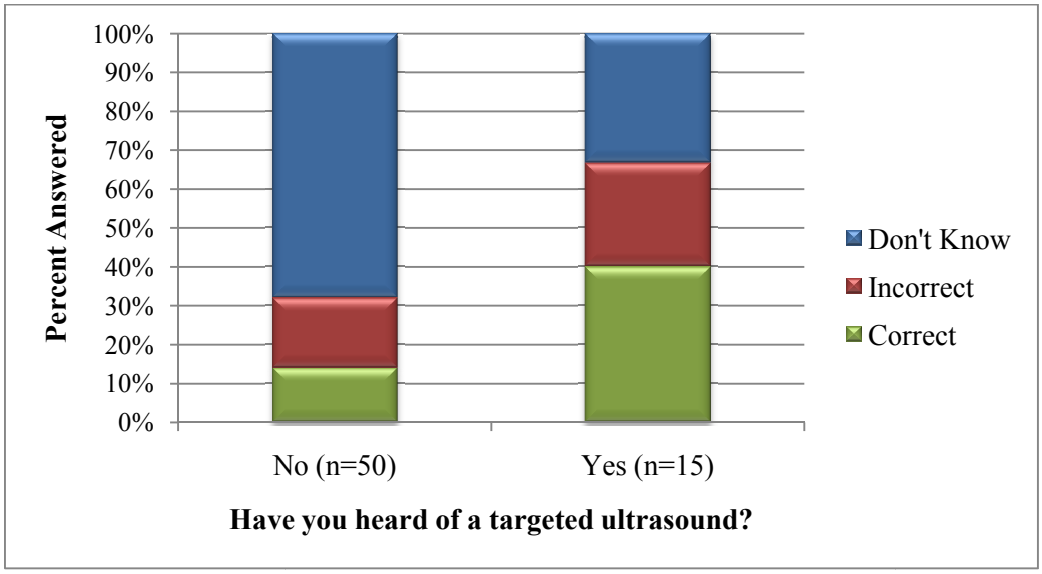
Answers to ultrasound knowledge questions regarding cleft lip, mental retardation, and chromosome problem(s) were significantly different. For answers regarding ultrasound's ability to detect cleft lip, women who had heard of a targeted ultrasound were more likely to answer correctly (Figure 12). A larger percentage of women who had heard of a targeted ultrasound answered the question regarding ultrasound's ability to detect mental retardation correctly compared to those who had not heard of targeted ultrasound.

Figure 12: Answers to Targeted Ultrasound's Ability to Detect Cleft Lip by Women Who Have Heard of a Targeted Ultrasound



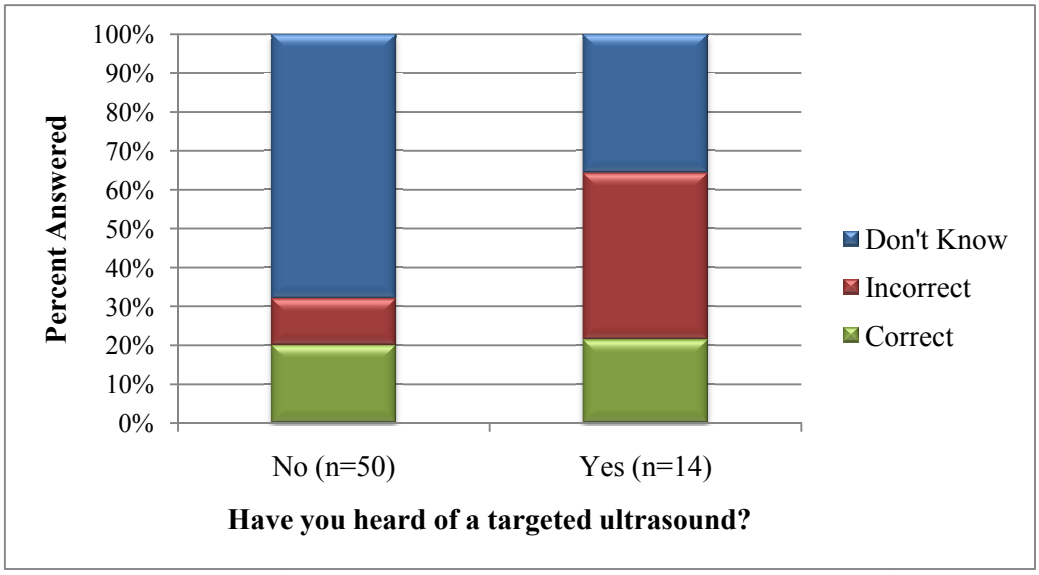
Although women who had previously heard of a targeted ultrasound answered the question correctly more frequently, this group also had a higher percentage of respondents choosing the incorrect answer compared to the other group. Women who had heard of a targeted ultrasound were more likely to choose an answer, whether right or wrong, as opposed to "don't know", which is a trend similar to that noted earlier among more educated participants (Figure 13).

Figure 13: Answers to Targeted Ultrasound's Ability to Detect Mental Retardation by Women Who Have Heard of a Targeted Ultrasound



In contrast to the above results, individuals who had heard of a targeted ultrasound were more likely to answer incorrectly for ultrasound's ability to detect chromosome problem(s) (Figure 14).

Figure 14: Answers to Targeted Ultrasound's Ability to Detect Chromosome Problem(s) by Women Who Have Heard of a Targeted Ultrasound



Of note, comparisons were made between responses from ultrasound knowledge questions and women who reported hearing of the targeted ultrasound from their doctor versus someone other than their doctor. There were no differences between the source of information and the respondents' answers.

Perception of Detection Rate of Down Syndrome by Targeted Ultrasound

Three of the questions on the questionnaire were designed to assess the participants' perception of the detection rate of Down syndrome by targeted ultrasound, referred to in this section as perception questions. Again, missing data was not used in calculations. Before determining perception, women were asked if they had heard of Down syndrome. Two women out of 77 had not heard of Down syndrome and 2 women answered "don't know." The remaining 73 women had heard of Down syndrome. The first question directed toward evaluating the participant's perspective stated: "A targeted ultrasound will be able to tell you if your baby has Down syndrome" (Q9). The answer choices included: never, rarely, sometimes, most of the time, always, and don't know. The second question (Q10) asked, "What percent of babies with Down syndrome will have an abnormal finding on a targeted ultrasound?" Finally, question three asked (Q11): "Does a "normal" targeted ultrasound result guarantee that the baby will be born without Down syndrome?" For the remainder of the results, the preceding three questions are referred to as Q9, Q10, and Q11. The results of these questions are found in Figures 15-17.

Figure 15: Q9: A targeted ultrasound will be able to tell you if your baby has Down syndrome.

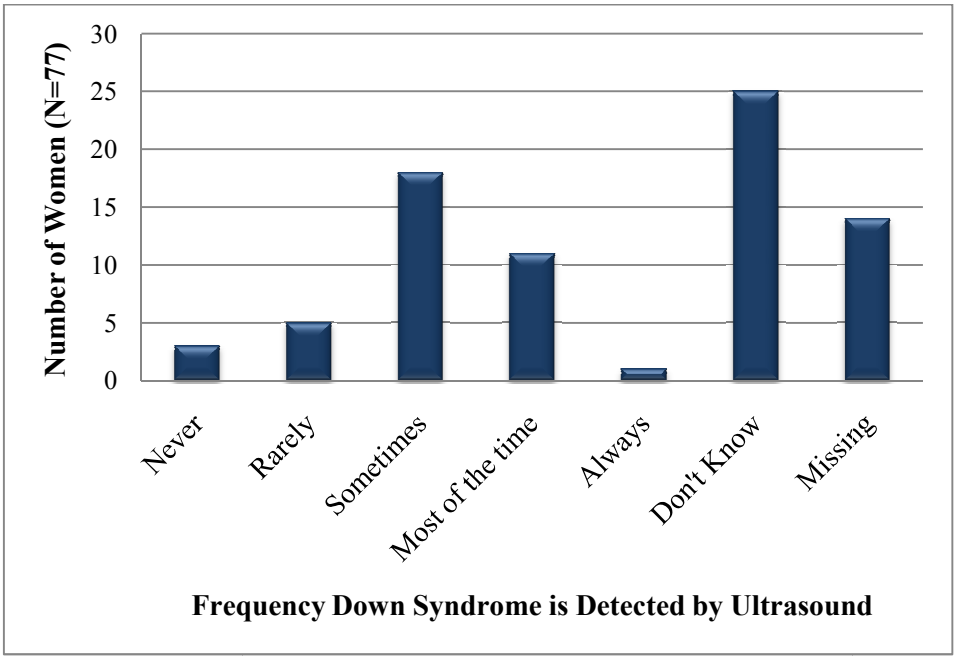


Figure 16: Q10: What percent of babies with Down syndrome will have an abnormal finding on a targeted ultrasound?

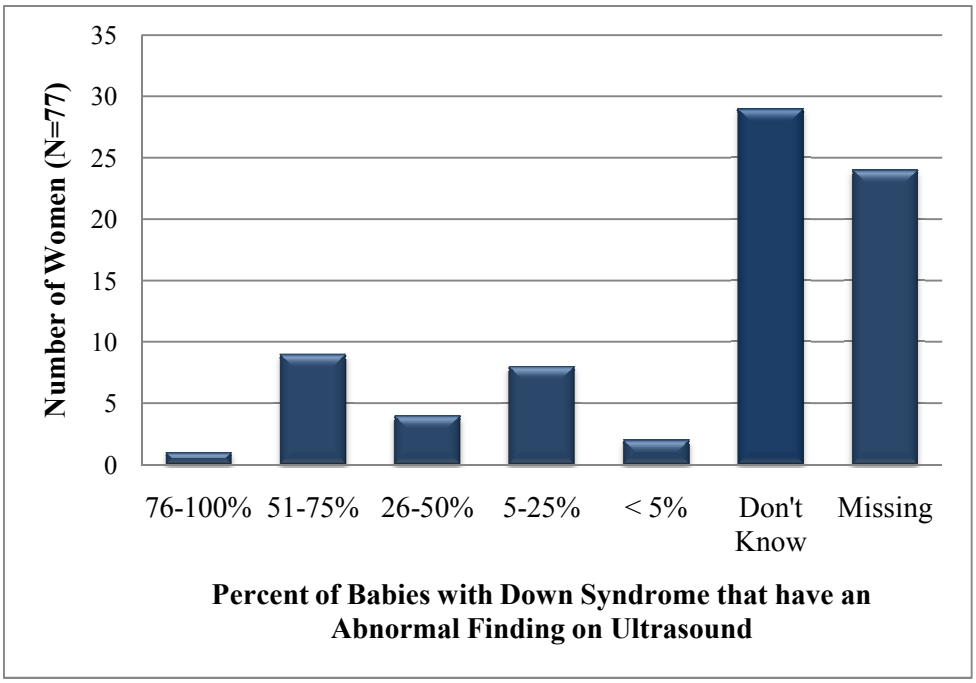
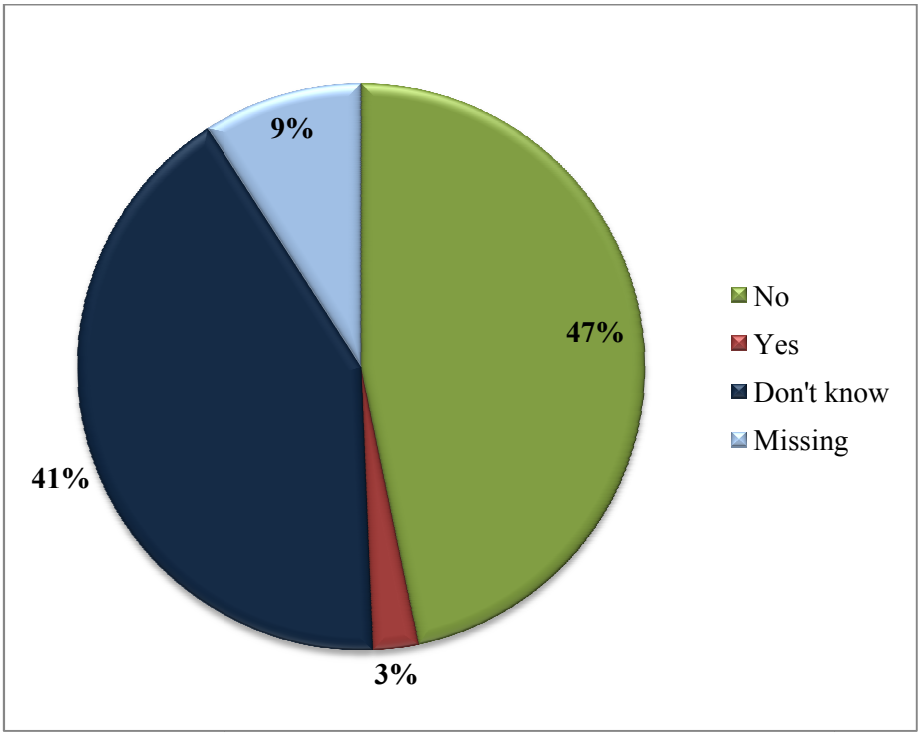
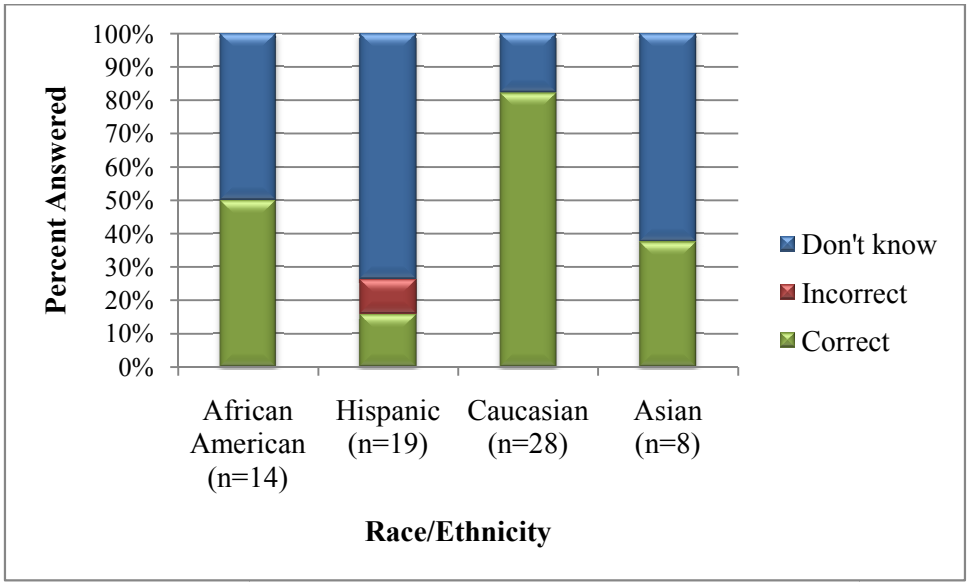


Figure 17: Q11: Does a "normal" targeted ultrasound result guarantee that the baby will be born without Down syndrome?



Answers to the three perception questions were compared to race/ethnicity for significance. Contingency tests between race/ethnicity and answers from women who had or had not heard of Down syndrome, Q9, and Q10 were not significant ($p>0.05$). However, Caucasians were more likely to answer Q11 correctly, answered "No," compared to Hispanics and African Americans (Figure 18).

Figure 18: Answers to Q11: "Does a "normal" targeted ultrasound result guarantee that the baby will be born without Down syndrome?" by Race/Ethnicity



(a) Significant difference between African American and Caucasian ($p=0.030$)

(b) Significant difference between Hispanic and Caucasian ($p<0.001$)

Contingency tests were also performed between education and perception questions. There were no significant differences between the answers from women who had or had not heard of Down syndrome, Q9, Q10, and Q11 ($p>0.05$).

Finally, the same questions were compared with whether or not participants had heard of a targeted ultrasound. As noted previously, participants that chose "no" or "don't know" to "have you heard of a targeted ultrasound" were combined into a single category, no. Results were not significant ($p>0.05$) for the following: "Have you heard of Down syndrome?" Q9, Q10, and Q11. When comparing women who had heard of the targeted ultrasound from their doctor versus someone other than their doctor, women were more

likely to answer Q11 correctly if they reported hearing of the targeted ultrasound from their doctor ($p=0.024$).

When comparing answers to the question "Have you heard of Down syndrome?" to answers for Q9, Q10 and Q11, no significant differences were found. Answers between Q9 and Q10 were significantly different ($p<0.001$). While, most women chose "don't know" for both questions, those who thought ultrasound would be able to detect Down syndrome at least some of the time (Q9), answered correspondingly to Q10. For example and individual who answered "most of the time" to Q9 was more likely to answer "51%-75%" to Q10. Responses between Q10 and Q11 were also significantly different ($p=0.003$), although the majority of responses were "don't know" for both questions.

Similarly to the analysis performed on ultrasound knowledge data, in an attempt to identify factors that most influenced participants' answers, responses were stratified by education and race/ethnicity. No overall trends were observed, but results from Q11 stratified by education and testing for differences between race/ethnicity was significant between Hispanics and Caucasians. Among individuals with less than a college degree, Hispanics were more likely to answer "don't know" and Caucasians were more likely to answer correctly.

Overall Accuracy

Results of perception questions were compared for accuracy. Of note, only 14.3% of individuals got 2 of the 3 questions correct; no one answered all three perception questions correctly. Ultrasound knowledge questions regarding detection of mental retardation and chromosome problem(s) were also included because of their relationship with Down

syndrome. With 5 questions pertaining to detection of Down syndrome by targeted ultrasound, 3.9% of participants got 4 out of 5 answers correct.

DISCUSSION

The purpose of this study was to determine the perception and knowledge of targeted ultrasound in women who screen positive for Down syndrome in the first or second trimester, and to assess the perceived detection rate of Down syndrome by targeted ultrasound in this population. It was hypothesized that women would not have an accurate perception and knowledge of the targeted ultrasound and its role in detecting Down syndrome. A total of 77 women participated in the study.

Previous studies have examined patient expectations and knowledge of routine ultrasound scans in the first and second trimester. In the past, surveys have been performed in Denmark (Larsen et al., 2000), the United Kingdom (Basama et al., 2004; Smith et al., 2004), Ireland (Lalor & Devane, 2007), Sweden (Eurenius et al., 1997), China (Chan et al., 2008), and Canada (Kohut et al., 2002). Due to cultural and institutional differences, the patient perceptions identified in their studies may not be applicable to the patient population in the United States, particularly in our clinics. In addition, there are no studies to date that examine the patients' knowledge of the targeted ultrasound and its ability to detect certain anomalies. Therefore, this cross-sectional, descriptive study is the first to compare the perceptions of high risk patients regarding the targeted ultrasound and its role in detecting specific ultrasound anomalies and Down syndrome.

Demographics

Demographic data obtained from the questionnaire was comparable to other studies performed in the same clinics (Czerwinski et al., 2010; Hoskovec et al., 2008). Overall,

significant differences among demographic variables showed typical trends. Individuals with a higher education were more likely to have a higher combined household income. Individuals of Caucasian or Asian ethnicity were more likely to earn a higher education. There is likely a positive feedback effect among families with a higher income capable of providing higher education as well as the fact that individuals with more education earn a higher salary.

Education and income are both indicators of socioeconomic status. For the purposes of further analysis, education was used as a comparison because it is a better measure of intrinsic ability to understand and synthesize information. Race/ethnicity was also used in order to tailor counseling provided to patients at different clinics with varied racial-ethnic populations.

Targeted Ultrasound Knowledge

In general, previous studies have shown that patient knowledge about ultrasound is unsatisfactory. This is supported by our study. On average, women answered ultrasound questions correctly 36% of the time and did not know the answer or did not answer the question 54% of the time. This is comparable with Chan et al. (2008) reporting 47% of patients could answer 13 of 19 questions regarding capabilities of a routine ultrasound correctly. Chan et al. (2008) study population included women attending either first or second trimester routine ultrasound exams. Their higher percentage of correct answers may reflect more exposure to the general expectations from a routine ultrasound compared to those associated with the targeted ultrasound our population was referred for. More than 50% of the participants in our study correctly answered detection of routine findings such as

due date, structure of heart, number of fetuses, and gender more frequently than other ultrasound knowledge questions. Previous studies are consistent with this finding keeping in mind that the previous studies were designed to assess perception and knowledge of routine ultrasound exams. Chan and colleagues determined 92% of their participants knew the purpose of the ultrasound was to identify fetal gender and 95% reported the use for visualizing fetal heart movement. Lalor et al. (2007) and Eurenius et al. (1997) both reported a good patient knowledge of ultrasound's ability to diagnose multiple pregnancies. In addition, the latter group reported patients having high expectations for confirming estimated date of confinement (Eurenius et al., 1997). Subsequently, participants in our study incorrectly answered ultrasound questions regarding detection of facial features of Down syndrome and the health of the baby. It has been reported that parents' main concern and motivation for ultrasound examination is to monitor the health of the baby (Eurenius et al., 1997; Lalor & Devane, 2007). Parents likely have reassurance based on the result of a "normal" ultrasound, although the actual health of the baby cannot be determined. The high percentage of incorrect answers for detection of facial features of Down syndrome is likely due to the fact that it refers to a structural aspect of the fetus. Although ultrasound is used to evaluate the structural anatomy of the fetus, including some specific facial structures such as nose and mouth (e.g. cleft lip), subtle features such as epicanthal folds and downslanting palpebral fissures are unable to be detected. This may be attributed to society's high expectations of modern medical technology, particularly with the more common use of 3-D and 4-D ultrasound.

Results revealed a difference between ultrasound knowledge and ethnicity. In general, Caucasians answered questions correctly more frequently than other groups. There

are several factors that may influence this affect. Social groups exist between individuals within racial groups that may expose one group to more information than another. In addition to access to information provided by social groups, individuals may have access to different resources such as the internet. Although the questionnaire was available in both English and Spanish, the vast majority (94%) were completed in English. It is possible that women who speak English as their second language received an English questionnaire, when they would have been more comfortable reading a Spanish version. This group of women is likely very small, but language barriers may have been present in this type of scenario. Finally, it has been well documented that Hispanics and African Americans are often late to receive prenatal care (Frisbie, Echevarria, & Hummer, 2001). It is possible that previous experiences either aid or hinder the ability to answer questions correctly.

There were three main trends observed when comparing answers to ultrasound knowledge and education level. One, individuals with higher education were more likely to answer correctly. Two, individuals with higher education were more likely to choose an answer, whether correct or incorrect. Finally, individuals with less education were more likely to choose "don't know" as an answer. A similar result was shown by Chan et al. (2008). They reported 92% of individuals with non-tertiary level of education had poor ultrasound knowledge compared to only 4% of individuals with a tertiary level. Of their population with a tertiary level of education, the majority of individuals were recorded as having a good knowledge of ultrasound. The findings were not surprising. Participants that had more education are probably more confident when choosing an answer because of previous experiences. It is reasonable to assume individuals with a college education or higher have had more exposure to questionnaires, exams, and making educated guesses.

There is also a higher chance that they can synthesize information and better understand the questions. On the other hand, participants reporting less than a college degree may feel that choosing "don't know" is a safer choice.

Finally, individuals who had previously heard of a targeted ultrasound answered the questions regarding ultrasound knowledge correctly more often. Also, individuals who reported previously hearing of a targeted ultrasound were more likely to have also had an accompanied discussion about the ultrasound or read additional information. Interestingly, participants who had heard of the targeted ultrasound were more likely to answer the question about ultrasound's ability to detect chromosome problems incorrectly. This may be due to a referral bias for these women. Under the assumption that they heard of the targeted ultrasound after learning of their positive screening result, it is possible they misinterpreted that the targeted ultrasound was recommended to determine if the baby had Down syndrome as opposed to evaluating the fetus for anomalies associated with an increased risk for Down syndrome.

Perception of the Detection Rate of Down Syndrome by Targeted Ultrasound

To date, no studies focusing on patient perception of the detection rate of Down syndrome by targeted ultrasound have been published. One study asked women if ultrasound could diagnose chromosomal abnormalities (e.g. Down syndrome). Forty-three percent of respondents answered correctly, 30% answered incorrectly, and 29% did not know the answer (Chan et al., 2008). Similarly, one in three women from Lalor and Devane's study population thought the ultrasound exam would detect Down syndrome and other chromosomal abnormalities (Lalor & Devane, 2007). In contrast to the previous

studies, we asked participants to answer how often they thought Down syndrome was diagnosed by ultrasound (Q9). Only 4% of our population answered the question correctly, choosing "never", while 45% answered incorrectly. The next question (Q10) was used to expose the difference between a diagnosis of Down syndrome and the detection rate by ultrasound. This question highlights the limitation of ultrasound and its purpose of identifying abnormal structures, as opposed to diagnosing underlying etiologies. Similar to the answers from Q9, only 12% of participants answered Q10 correctly, and 19% answered the question incorrectly. The remaining individuals either answered "don't know" or did not answer the question. It is clear that our patient population did not have good background knowledge of ultrasound as it pertains to detecting Down syndrome. In contrast to the prior to questions, participants had a higher accuracy when responding to the third perception question (Q11), although there was still a large percentage of individuals that chose "don't know." It appears women better understand that ultrasound cannot offer any guarantees and that problems may still exist. This was also seen in a study by Smith et al. (2004) when patients were asked "If the scan is normal, the baby might still have a problem." Seventy-eight percent of their participants correctly understood this statement to be true. Our population had a more difficult time answering questions that were more knowledge-based requiring a basic understanding of medical terminology.

Overall, we were not able to determine if women over or under-estimated the capabilities of targeted ultrasound when detecting Down syndrome, because there was a wide range of answers to the questions and an even larger percentage of individuals reporting that they did not know the answer. It seems that our patient population lacks background knowledge to form an initial perception. Answers to Q9 indicate an over-

estimation of ultrasound's ability as few women knew that ultrasound would never diagnose Down syndrome. The answers to this question may represent an underlying comprehension issue. Women may not understand the difference between diagnosing a chromosome problem versus identifying abnormal findings on ultrasound that suggest an underlying chromosome problem.

To determine the level of background knowledge of targeted ultrasound we assessed how often combinations of questions were answered correctly by a single participant. By and large, our study population's ultrasound knowledge was limited. Only 14% of our participants could answer 2 out of the 3 perception questions (Q9, Q10, Q11) correctly. When we added ultrasound knowledge questions related to Down syndrome, including the detection of mental retardation and chromosome problems by ultrasound, only 4% of our study population answered 4 out of 5 questions correctly. Although it is unrealistic to assume individuals in the general population would accurately answer all of the questions, it is surprising to see that such a low percentage answered a combination of the questions correctly. In general, the results from our study display a limited amount of background knowledge in our referral population.

Additional Factors to Consider

It is important to explore the effect of stress and/or anxiety as it relates to the ability to complete questionnaires in a clinical setting such as ours. Studies show women experience anxiety after receiving a positive serum screen result for Down syndrome (Marteau et al., 1992; Weinans et al., 2000). In addition, acute stress causes several adverse affects such as: impaired ability to retrieve memories, limited attentional resources

(increased selective attention), and sub-optimal decision making (Buchanan, Tranel, & Adolphs, 2006; Chajut & Algom, 2003; Keinan, 1987). While filling out the questionnaire prior to genetic counseling, it is possible that one or multiple of these adverse affects played a role in the ability of the participant to accurately complete the questionnaire. These factors are more likely to play a role in the results of this study compared to those that were previously mentioned, such as Chan et al. (2008), because the other patient populations completed the questionnaires or studies while attending routine ultrasound exams and were not referred due to a high risk indication. It is important to keep this in mind while counseling patients in order to provide detailed, important information in a simple, understandable manner. This is crucial for patient autonomy and informed decision making.

Larsen and colleagues make an argument that information provided to pregnant women prior to ultrasound examinations is insufficient (Larsen et al., 2000). Previously, it was suggested that women undergo ultrasound because it has been integrated as a routine part of prenatal care as opposed to making an informed decision (Mitchell, 2004). Our study reinforces that patient knowledge of targeted ultrasound and its role in detecting Down syndrome is poor, which raises the question: how "informed" of a decision are our patients making? As ultrasound's role in prenatal care continues to evolve, it is of utmost importance that women are informed of the limitations, as well as the purpose of the ultrasound, to avoid false expectations and equip women with information that may prepare them for a problem identified by ultrasound.

Limitations and Future Studies

There are limitations in this study that are related to a self-administered questionnaire and small sample size. There was no reliability or internal validity tests performed on the questionnaire. It was created by the committee and piloted among genetic counselors to test understanding and clarity. There was missing data that is a common problem seen in self-administered questionnaires. The small sample size of our study prevented statistical support to confirm trends observed in the data. Questions evaluating patient knowledge, designed to aid in appropriate counseling, may misrepresent a patient's actual understanding. The participant may have the correct information regarding the detection rate of Down syndrome or other ultrasound findings by ultrasound but be unable to recall the answer at the time of the appointment. It is also possible that friends or family, if present when the respondent was filling out the questionnaire, may have influenced their answers on the questionnaire.

As medical technology and diagnostic capabilities of ultrasound continue to evolve over time, patient perceptions will also change. It is important to continuously evaluate patient knowledge in efforts to improve counseling and acknowledge patients' right to informed consent. Future studies of interest include a before and after questionnaire to evaluate the usefulness of the genetic counseling session as it pertains to patients' knowledge of targeted ultrasound. An evaluation of patients' decisions regarding invasive testing in light of their knowledge of targeted ultrasound would be helpful to assess if their perception has an effect on their decision. Finally, a review of the available sources of education about targeted ultrasound and a study to examine if one education technique such as written information, counseling session, or internet is more effective than others.

Conclusion

Prior to genetic counseling, women do not have an accurate knowledge of the targeted ultrasound and its role in detecting Down syndrome. There is a general lack of understanding that prevents individuals from having the ability to form a perception. It is imperative to assess perception and discuss the purpose and limitations of the targeted ultrasound with patients prior to ultrasound examinations. Providing appropriate information to our patients will equip them with the tools to make an informed decision about the ultrasound and any additional diagnostic or screening tests.

APPENDIX A

University of Texas-Medical School at Houston

Knowledge and Perception Down syndrome and Targeted Ultrasound

Instructions: Please read each question and mark your answer. Try to answer every question as best you can. Thank you.

Targeted Ultrasound Information:

Targeted ultrasound is a special ultrasound during the second trimester of pregnancy that looks at the baby's organs. This ultrasound is also referred to as an anatomy scan, level II ultrasound, or genetic ultrasound.

1. Have you had an ultrasound of any kind during this pregnancy?
   (A) Yes
   (B) No
   (C) Don't know

   a. If yes, how many? _____

2. Have you heard of a targeted ultrasound?
   (A) Yes
   (B) No
   (C) Don't know

   a. If yes, where did you hear about the targeted ultrasound?
      (A) Family
      (B) Friend
      (C) Internet
      (D) Doctor
      (E) Brochure
      (F) Other: _____

3. How many targeted ultrasounds have you had prior to today in any pregnancy (current or past)?
   (A) 0
   (B) 1
   (C) 2
   (D) 3

(E) 4
(F) 5 or more

4. How many total pregnancies have you had (including the current one)?
   (A) 1
   (B) 2
   (C) 3
   (D) 4
   (E) 5 or more

5. How many living children do you have?
   (A) 0
   (B) 1
   (C) 2
   (D) 3
   (E) 4
   (F) 5 or more

6. Have you had a child with a genetic condition or birth defect?
   (A) Yes
   (B) No

      a. <u>If yes</u>, what was the name of the genetic condition or birth defect?
         _____

7. Do you know anyone (friends/relatives/coworkers) who has a child or a personal history of a genetic disorder or birth defect?
   (A) Yes
   (B) No
   (C) Don't know

      a. <u>If yes</u>, what condition or birth defect did they have? _____

8. Have you heard of Down syndrome?
   (A) Yes
   (B) No
   (C) Don't know

9. A targeted ultrasound will be able to tell you if your baby has Down syndrome.
   (A) Never
   (B) Rarely
   (C) Sometimes
   (D) Most of the time
   (E) Always

10. What percent of babies with Down syndrome will have an abnormal finding on a targeted ultrasound?
    (A) 76-100% of babies
    (B) 51-75% of babies
    (C) 26-50% of babies
    (D) 5-25% of babies
    (E) <5% of babies

11. Does a "normal" targeted ultrasound result guarantee that the baby will be born without Down syndrome?
    (A) Yes
    (B) No
    (C) Don't know

12. With the understanding that ultrasound may be limited by gestational age and position of baby, in most cases, **it is <u>possible</u> for a targeted ultrasound to detect any of the following in the baby**.

    Circle <u>one</u> answer for each question.

a.	Cleft lip	YES	NO	DON'T KNOW
b.	Function of baby's brain	YES	NO	DON'T KNOW
c.	Due date	YES	NO	DON'T KNOW
d.	Structure of heart	YES	NO	DON'T KNOW
e.	Spina bifida	YES	NO	DON'T KNOW
f.	Mental retardation	YES	NO	DON'T KNOW
g.	Number of babies (single v. twin)	YES	NO	DON'T KNOW
h.	Health of baby	YES	NO	DON'T KNOW
i.	Chromosome problem(s)	YES	NO	DON'T KNOW
j.	Facial features of Down syndrome	YES	NO	DON'T KNOW
k.	Kidney structure	YES	NO	DON'T KNOW
l.	Signs of Down syndrome	YES	NO	DON'T KNOW

m. Gender of baby YES NO DON'T KNOW

n. Autism YES NO DON'T KNOW

o. Structure of brain YES NO DON'T KNOW

13. Please circle the **<u>one answer</u>** that best describes your race/ethnicity, or fill in with the appropriate response.
    (A) African-American
    (B) Hispanic
    (C) Asian
    (D) Caucasian
    (E) Other _____

14. What is the highest grade you have completed?
    (A) Some high school
    (B) High school
    (C) Some college
    (D) Bachelor degree
    (E) Post-graduate or professional degree

15. What is your household's combined annual income?
    (A) < $10,000
    (B) $10,000-$25,000
    (C) $25,000-$50,000
    (D) $50,000-$75000
    (E) $75,000-100,000
    (F) >$100,000

Thank you for your time!

APPENDIX B

The University of Texas Medical School – Houston
Knowledge and perception of Down syndrome and targeted ultrasound

Dear Potential Study Participant,

You are being invited to take part in a research study conducted by Ashley Henriksen and Jennifer Hoskovec at the University of Texas Medical School Houston. We are interested in determining what you think ultrasound can tell you about Down syndrome. Women have different perceptions of the ultrasound and the capabilities of an ultrasound to detect Down syndrome. A targeted ultrasound is a detailed ultrasound examination interpreted by a Maternal Fetal Medicine Specialist. It is helpful for doctors and genetic counselors to know what patients think about ultrasound.

Your decision to join this research study is voluntary. You may refuse to take part, or choose to stop taking part at any time. Your decision about participation in this study or answering questions will not change the care or services that are available to you now. This research project has been reviewed and approved by the Committee for the Protection of Human Subjects (CPHS) of the University of Texas Houston Health Science Center.

If you agree to participate in this study, you will be asked to complete a questionnaire before your genetic counseling session. You will be asked about your age, race/ethnicity, education, previous pregnancies, and questions about ultrasound and Down syndrome. The questionnaire will take approximately 10-15 minutes to complete. Your responses will be confidential and will be viewed only by the researchers involved in the study. After completing the questionnaire, it will be placed in a sealed envelope for the investigators.

Although the results of this study will be useful for doctors, other health professionals, and future pregnant women, there may be no direct benefit to you for participating in this study. There are no known risks to you for participating in this study. You can choose not to take part in this study at any time. If you decide to participate, it is very important that you answer as honestly as you can to the questions that are asked. There are no additional costs to you to participate in this study. No personal identifiers will be recorded for the purpose of this research study.

If you have any questions regarding this research study, please contact Ashley Henriksen, BS, or Jennifer Hoskovec, MS, CGC at (713) 500-6383. If you are willing to take part in our study, please complete and return the questionnaire in the enclosed envelope to the front desk personnel or genetic counselor.

Thank you very much for considering this invitation to participate in our study.

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VITA

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