HERC Coverage Guidance – Prenatal Genetic Testing
Disposition of Public Comments

Table of Contents

Commenters 1

Public Comments Grouped by Topic 2

- Invasive Aneuploidy Testing 2
- Cell Free Fetal DNA Testing 2
- Noninvasive Aneuploidy Testing 9
- Carrier Screening 11
- Genetic Counseling 11

References Provided by Commenters 14

Commenters

Identification	Stakeholder
A	*Oregon Medicaid Managed Care Medical Director*
B	*Verinata Health,* Redwood City, CA
C	*7 Physicians and 4 Genetic Counselors,* Legacy Medical Group- Maternal Fetal Medicine, Portland, OR
D	*6 Physicians and 4 Genetic Counselors,* OHSU, Portland, OR
E	*10 Portland-area Prenatal Genetic Counselors from the following organizations:* OHSU Dept. of OB/GYN, Division of Maternal Fetal Medicine Women's Health Associates, LLC, Northwest Perinatal Center Legacy Emanuel Hospital Maternal Fetal Medicine

DRAFT

Public Comments Grouped by Topic

Stakeholder	#	Comment	Disposition
Invasive Aneuploidy Testing			
A	1	Comments regarding the prenatal genetic testing draft: A concern regarding universally offering genetic counseling and invasive aneuploidy testing for any woman over 34 years old, even if noninvasive screening is normal. Given funding priorities, and that this is a "weak" recommendation, is it appropriate for OHP benefits? Should this be reset to an older maternal age with a higher pretest probability of aneuploidy in the presence of negative screening? Unless you have good evidence to support counseling and invasive testing for mothers > 34 who have a negative noninvasive screen, it seems to me that should not be covered given the priorities of OHP funding.	EbGS agrees that the evidence pertaining to maternal age >34 does not warrant genetic counseling without additional indications of elevated risk. Guidance recommendation changed to reflect this.
A	2	Our Managed Care Plan is seeing tests beyond karyotyping requested (e.g. microarrays) as a routine for advanced maternal age, by the OHSU obstetrics/genetics group.	Guidance document only recommends coverage of array CGH if major fetal anomalies are apparent on imaging and karyotype is normal.
Cell Free Fetal DNA Testing			
B	3	We are writing in response to your Draft Coverage Guidance: Prenatal Genetic Testing, more specifically *Cell Free Fetal DNA Testing*. The proposed position of HERC is to NOT recommend coverage for the aforementioned type of prenatal testing due to 'no evidence identified' in support of its use. Please review the following and accompanying information as provided evidence in support of Cell Free Fetal DNA Testing and its use: **Technology Assessments** ***Sequencing-Based Tests to Determine Fetal Trisomy 21 from Maternal Plasma DNA*, April 2013; Technology Evaluation Center (TEC): Blue Cross Blue Shield** Association's Office of Clinical Affairs in conjunction with Kaiser Permanente Medical Care Program. Evaluation criteria include, 1) The technology must have final approval from the appropriate governmental regulatory bodies; 2) The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes; 3) The technology must improve the net health outcome; 4) The technology must be as beneficial as any established alternatives; and, 5) The improvement must be attainable outside the investigational settings. **Conclusion: '**Based on the above, nucleic acid sequencing-based testing of	This citation is from one of the HERC trusted sources and indeed concluded that cell-free DNA testing for trisomy 21 meets TEC criteria for coverage in both high-risk and average risk women, based on 9 studies. Only one of these addressed average risk women. EbGS agrees that the evidence is sufficient to recommend coverage of cell-free fetal DNA testing in high-risk women, but not in average risk women. Guidance recommendation changed to reflect this.

DRAFT

Stakeholder	#	Comment	Disposition
		maternal plasma for trisomy 21 with confirmatory testing of positive results (as is expected to be performed in a real-world clinical setting) in both high-risk women and average-risk women being screened for trisomy 21 meets the TEC criteria.'	
B	4	***Fetal Aneuploidy Detection by Maternal Plasma DNA Sequencing, Part 2,* October 2013; California Technology Assessment Forum (CTAF).** Evaluation criteria: same as TEC (above). **Recommendation #1**: 'It is recommended that the use of cell free fetal DNA as a prenatal advanced screening test for fetal aneuploidy for Trisomy 21 and Trisomy 18 in high risk women meets CTAF criteria 1-5 for safety and efficacy and improvement in health outcomes.' **Conclusion: '**In conclusion, cffDNA is a promising new technology with high sensitivity and specificity for the prediction of fetal aneuploidy, in particular T 21 and T18, when evaluated as an advanced screening test in high risk women. In high risk women, when used as an advanced screening test, it has the potential to reduce the number of invasive diagnostic procedures, with their associated risks of fetal loss.**'**	This TA (dated June 2012) also concludes that cell-free DNA testing for trisomy 21, 18 and 13 meets TEC criteria for coverage in high-risk women, based on 7 studies. See comment #3.
B	5	**Professional Society Recommendations/Position Statements:** The following societies have reviewed cell free fetal DNA testing technology and have adopted cautionary yet favorable positions on its use in the clinical setting. **American College of Obstetricians and Gynecologists/Society for Maternal-Fetal Medicine (ACOG/SMFM): Committee Opinion 545: Noninvasive Prenatal Testing for Fetal Aneuploidy, Dec. 2012**	ACOG recommendations state the following: *Patients at increased risk of aneuploidy can be offered testing with cell free fetal DNA. This technology can be expected to identify approximately 98% of cases of Down syndrome with a false-positive rate of less than 0.5%.* AND *Cell free fetal DNA testing should not be offered to low-risk women or women with multiple gestations because it has not been sufficiently evaluated in these groups.*
B	6	**International Society for Prenatal Diagnosis (ISPD): Position Statement from the Aneuploidy Screening Committee on Behalf of the Board of the International Society for Prenatal Diagnosis, April 2013.**	This guideline states: *Although rapid progress is being made in the development and validation of this technology, demonstration that in actual clinical practice the testing is sufficiently accurate, has low failure rates and can be provided in a timely fashion has not yet been provided.* They list 9 caveats highlighting the test limitations: *1. Reliable non-invasive maternal cf DNA aneuploidy screening methods have only been reported for trisomy 21 and 18. cfDNA*

DRAFT

Stakeholder	#	Comment	Disposition
			screening results have been reported for trisomy 13 but the numbers are not large and efficacy appears to be less than for trisomies 21 and 18. cfDNA screening results have also been reported for sex chromosome aneuploidy and the efficacy is unacceptably low *2. There are insufficient data available to judge whether any specific cfDNA screening method is most effective* *3. The tests should not be considered to be fully diagnostic and therefore are not a replacement for amniocentesis and CVS. Some affected pregnancies may not be detected and there may be false-positive results.* *4. Analytic validity trials have been mostly focused on patients who are at high risk on the basis of maternal age or other screening tests. Efficacy in low risk populations has not yet been fully demonstrated. There are currently only limited data to suggest the test failure rate will not be appreciably higher for low-risk women and the false-positive rate also appears to be comparable.* *5. There is insufficient information to know how well the test will perform in multiple gestation pregnancies that are discordant for trisomy but, theoretically, the detection of affected pregnancies could be lower than in singletons. When there has been a known early demise of a co-twin ("vanishing twin"), results may be inaccurate.* *6. In cases where mosaicism is present (including confined placental mosaicism) results may be inaccurate.* *7. In a proportion of cases there is insufficient fetal cfDNA in the maternal plasma specimen or there is test failure for other reasons (Table 2). It is not known what proportion of women with insufficient fetal cfDNA or a failed or uninterpretable test would have an informative repeat test result. In addition, one of the cfDNA screening methods classifies a proportion of results as "unclassified" when they are in fact at somewhat increased risk of aneuploidy.* *8. Specific independently developed laboratory minimum standards, quality control, proficiency testing and inspection requirements have not yet been developed for this testing. It is expected that quality control standards will be developed and the ISPD strongly cautions*

DRAFT

Stakeholder	#	Comment	Disposition
			providers to seek out laboratory services that meet national guidelines for quality control and proficiency testing that is the current standard for other molecular tests. *9. It has not been demonstrated that the test can be provided in a cost-effective, timely, and equitable manner to total populations.*
B	7	**National Society of Genetic Counselors: Noninvasive Prenatal Testing/Noninvasive Prenatal Diagnosis: the position of the *National Society of Genetic Counselors***	This position statement of the NSGC, dated April 2012, states: *NSGC does not currently support NIPT as a routine, first-tier aneuploidy screening test in low-risk populations: To date, these technologies have been validated only in pregnancies considered to be at an increased risk for fetal aneuploidy, based on maternal age, family history, or positive serum and/or sonographic screening tests.* *Clinical studies show that MPS (massively parallel sequencing) effectively detects fetal trisomy 21, trisomy 13, and trisomy 18. MPS has not yet been proven efficacious in detecting other chromosomal abnormalities or single-gene disorders, and clinical trials for other technologies have not yet been published. NSGC recommends that pretest counseling for NIPT include information about the disorders that it may detect, its limitations in detecting these conditions, and its unproven role in detecting other conditions.*
B	8	**Oregon's Commercial Insurance Reviews and Coverage** In addition to the aforementioned favorable assessments and clinical professional societal recommendations, the national and regional payers have completed reviews of the Cell Free Fetal DNA Testing technology and found their use to be medically necessary and a covered benefit under their health plan offerings. Those payers with positive medical policy and coverage for Cell Free Fetal DNA testing and operating within Oregon include: • Aetna • Coventry • Humana • Health Net • UnitedHealthcare • Regence BCBS of Oregon	Thank you for providing this information. The EbGS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies.

DRAFT

Stakeholder	#	Comment	Disposition
		• Providence Health Plan • ODS Health Plans • Lifewise of Oregon	
B	9	**Costs** While this test could be looked at as additive to the current prenatal screening care continuum and as such the program would incur increased costs, there is data and information to suggest that the utilization of the Cell Free Fetal DNA Testing could be off-set by the decrease in utilization of invasive procedures such as CVS and amniocentesis. Additionally, should there be unfavorable outcomes associated with the continued utilization of invasive procedures, costs associated with those outcomes can compound cost significantly; these unfavorable outcomes and associated costs could be mitigated with the inclusion of Cell Free Fetal DNA Testing in the prenatal care continuum. A study addressing both the utilization and cost impact of Cell Free Fetal DNA Testing is also attached. This study was conducted by Bridgehead International and is titled, *Clinical and Cost Consequences of Incorporating a Novel Non-Invasive Prenatal Test into the Diagnostic Pathway for Fetal Trisomies;* Journal of Managed Care Medicine, Nov. 2012.	This cost model assumes a cost for the cell-free DNA test (verifi™) of $1200. Costs for other cffDNA tests range from $795 to $1900. Authors modeled a population of 5 million with 100,000 pregnancies annually. Model found a 66% reduction in invasive diagnostic induced miscarriages and that 38% more women received a T21 diagnosis. The model predicts that total costs for prenatal screening and diagnosis for fetal aneuploidies are reduced by 1% annually.
B	10	As a purveyor of one of the Cell Free Fetal DNA Testing options available to providers for prescribing to patients, we feel that in order to provide access and continuity of care across all populations residing in Oregon, HERC should adopt a favorable position on Cell Free Fetal DNA Testing and allow for its use. Thank you in advance for your review of the accompanying information of evidence support of Cell Free Fetal DNA Testing.	Thank you for your comments.
E	11	We are writing this letter in support of coverage for Non Invasive prenatal testing (NIPT) through cell free fetal DNA. While we applaud the Health Evidence Review Commission's decision to recommend coverage of aneuploidy screening, we disagree with the decision not to cover NIPT. The American College of Obstetrics & Gynecology and the Society for Maternal Fetal Medicine have both recommended noninvasive prenatal testing (NIPT) as a screening test for high-risk women. The National Society of Genetic Counselors and the International Society of Prenatal Diagnosis have also stated their approval of NIPT as an option for patients whose pregnancies are considered to be at an increased risk for certain	See comments #5, 6, and 7. Society for Maternal Fetal Medicine recommendations not cited or provided.

DRAFT

Stakeholder	#	Comment	Disposition
		chromosome abnormalities.	
E	12	Without NIPT women whose pregnancies are at high risk (advanced maternal age, abnormal serum screening, abnormal ultrasound findings, pregious pregnancy with aneuploidy) must choose between screening tests with lower detection rates and higher false positive rates versus an invasive procedure that may cause miscarriage. Furthermore, NIPT can be performed at any time in pregnancy after ~10 weeks gestation, providing valuable risk assessment information for women who may be outside of the recommended gestational age for any form of screening or invasive procedure.	Use of cffDNA testing does not necessarily obviate the need for invasive testing, since a positive result requires confirmation by CVS or amniocentesis. Also, cffDNA is only used to screen for trisomy 21 and 18. Women at high risk may still require additional testing. See comment #3.
E	13	Although not considered diagnostic, NIPT has been shown as a cost-effective tool in several U.S. studies. Studies by Song et al. (2013) and Ohno & Caughey (2013) have both shown that NIPT leads to improved detection of chromosome abnormalities with fewer false positives, fewer unnecessary invasive procedures, and lower rates of miscarriage in chromosomally-normal pregnancies. These studies have shown that in high-risk pregnancies (advanced maternal age, abnormal serum screening, abnormal ultrasound findings, previous pregnancy with aneuploidy), NIPT has lower total healthcare expenditures. For example, Song et al. estimated that NIPT would cost $300,000,000 less than first trimester screening and $500,000,000 less than traditional maternal serum screening.	Song 2013 is a CEA that modeled NIPT in women who were > 35 or those with a + conventional screening test, compared to first trimester screen and integrated screening method. Theoretical cohort was all US births in one year. Cost of test was $795 in the model. Other tests cost more, with MaterniT21™ being the most expensive at $1900. Ohno 2013 concludes that, in high risk women, NIPT used as a screening tool that requires invasive confirmation is more cost-effective than when it is used as a diagnostic tool (no confirmation, reproductive decision made based on NIPT only) and results in more false positive terminations than the number of procedure related losses in the those who undergo the invasive confirmation.
C	14	Cell Free Fetal DNA (cffDNA) testing We agree that cffDNA has not been evaluated as a primary screening test and should not be utilized in the general population or in multiple gestations at this time. However, there is quality evidence to support its use as an "advanced" or second line screening test. In such pregnancies (i.e. abnormal screening result), the use of cffDNA offers higher detection rates and lower false positive rates than historically utilized options. There is ample evidence to conclude cffDNA can detect 97-99% of pregnancies affected by either Down syndrome or Trisomy 18 in particular while maintaining a very low chance for a false positive result. Other conditions can also be detected, although this is currently based on lesser data.11-18	4 of the listed citations were included in the BCBS TEC assessment (see comment #3). One is the ACOG committee opinion (see comment #5) and one is the ISPD position statement (see comment #6). One is the ACMG statement on cffDNA: No direct recommendation is made, but the conclusions states: "The ACMG encourages providers of NIPS technology to make serious efforts to provide the more clinically relevant metrics—PPV and NPV. …. The ethical principle of distributive justice causes us to reflect on who will pay for NIPS and who should be insured for the procedure. No doubt NIPS costs will come down; however, for NIPS to establish roots in the perinatal aneuploidy screening paradigm, cost as a barrier to population-based screening must be minimized."

DRAFT

Stakeholder	#	Comment	Disposition
			The last citation is a fact sheet created by the National Coalition for Health Professional Education in Genetics and the National Society of Genetic Counselors.
C	15	CffDNA testing has been found to be a highly desired option for those women who do not wish diagnostic testing by CVS or amniocentesis. Declining to cover cffDNA testing forces families to either accept an option with a higher procedure related risk for loss or delaying testing until after delivery. We believe that cffDNA tests should be available to women who have a high pretest probability for positive findings (i.e. positive aneuploidy screen, enlarged NT measurement, or a structural anomaly on anatomic assessment of the fetus).19-22	Citation #19 is a SR of "factors influencing clinical use of NIPT". Included 11 studies pertaining to attitudes and experiences with using the test, makes the following suggestion: "Consideration needs to be made with respect to the needs of specific patient groups before the introduction of NIPT into clinical practice. For example, although it may be appropriate to offer NIPT in high risk pregnancies, introduction for population screening may not be warranted without further research, public consultation and discussion at policy level to address concerns about the ethical and social implications." Citation #20 is cohort study of women and health professionals that compared preferences between those groups for test attributes. They found women value avoidance of miscarriage most, while health professionals value accuracy most. Citation #21 is a narrative review and editorial that states "Although currently being integrated in some settings as a primary screening test for women at high risk of fetal aneuploidy, from a population perspective, a better option for noninvasive prenatal testing may be as a second-tier test for those patients who screen positive by conventional aneuploidy screening. How noninvasive prenatal testing will ultimately fit with the current prenatal testing algorithms remains to be determined. True cost–utility analyses will be needed to determine the actual clinical efficacy of this approach in the general prenatal population." AND "The absence of guidelines for quality control and quality assurance for the laboratory testing is a significant concern. The methodologies are highly complex and the testing is subject to intense commercial competitive pressures." AND

DRAFT

Stakeholder	#	Comment	Disposition
			"In a recent publication on noninvasive prenatal testing in an average risk population of women undergoing first-trimester screening, noninvasive prenatal testing detected 55% of the total chromosomal abnormalities (eight of eight cases of trisomy 21 and two of three cases of trisomy 18), whereas first trimester screening detected 100% (all T21 and T18 as well as seven other deletions, duplications, and other abnormalities). Citation #22 is a best ethical practices statement funded by the NIH that makes 10 recommendations and concludes "Principal recommendations include the amendment of current informed consent procedures to include attention to the noninvasive nature of new testing and the potential for a broader range of results earlier in the pregnancy. We strongly recommend that tests should only be provided through licensed medical providers and not directly to consumers."
C	16	Some groups argue that cffDNA testing should also be used as a first line test for women of advanced maternal age. Until there is sufficient evidence to support the use of cffDNA as a primary screening test and proven to be cost effective, we do not support this policy. We recommend that all women interested in screening, regardless of age, be offered conventional screening and be offered cffDNA based testing (in addition to diagnostic testing) only in the event of a positive screen result. All positive cffDNA results should be confirmed by traditional diagnostic testing due to the risk for false positive results.	Thank you for your comment.
Noninvasive Aneuploidy Testing			
C	17	While we recognize that the task of narrowing choices for testing is arduous, we feel that optimal patient care requires us to ask for the inclusion of additional options. Timing is important as some couples when faced with information that can impact the long term health of an individual, may decide not to continue a pregnancy. Diagnostic testing (chorionic villus sampling (CVS) or amniocentesis) is available under the current recommendations. However, the recommended options for screening severely limit first trimester screening capabilities. Thus, the option for CVS is significantly curtailed.	Thank you for taking the time to comment.

DRAFT

Stakeholder	#	Comment	Disposition
C	18	Aneuploidy screening: The commission has recommended four modalities. They have not commented on combined first trimester screening alone. The recommended methodologies might incorporate first trimester assessment of the nuchal translucency (NT) or in combination with serum analytes. However, the chosen methods either limit the capabilities of the first trimester screen (to limit false positive rates) or ignore it altogether. The bulk of the chosen methods delay full interpretation of risk until after 16 weeks, when first trimester diagnostic procedures opportunities have passed. This limits couple's choices and is incongruous with the commission's recommendation for CVS after a positive aneuploidy screen. We recommend combined first trimester screening (NT with HCG and PAPP-A) be added as a standalone screening option due to its high sensitivity, clinical availability, relatively low cost, and fast turnaround time in an early gestational window which would allow for counseling and further testing if desired.1-6	EbGS agrees that the first trimester screening option outlined in the NICE guideline should be one of the available screening options. Guidance recommendation changed to reflect this.
C	19	Screening with Ultrasound (US) The commission recommends anatomic assessment at 18-20 weeks, but does not comment on the use of first trimester US (particularly the assessment of the nuchal translucency). First trimester US provides important clinical information including: screening for structural anomalies, aneuploidy and/or genetic syndromes; providing early assessment of dating and viability (far more accurate than other clinical means); early recognition of multiple pregnancies including chorionicity, and detection of mullerian anomalies. Enlarged nuchal translucency (NT) measurements >95% for gestational age are known to increase the possibility for aneuploidy or structural anomaly, and NT measurements >99% also increase the risk for genetic syndromes as well. We recommend the option of NT measurements in all pregnancies in order to guide risk assessment for these issues. 7-10	NT is an element of stepwise sequential and contingency screening. Citations: #7 Ayras was a case series of 1063 pregnancies with increased NT. During the time period of this study, no biochemical 1st trimester screening tests were utilized. 78% of these fetuses had normal karyotype, but of those, 9% had structural defects or genetic disorders. #9 Mula is an abstract and editorial of a case series examining outcomes of 171 pregnancies with increased NT and normal karyotype. Of these, 28% did not survive due to miscarriage, termination or post natal death. Of the remaining infants, 10% had structural defects and 4% had severe neurodevelopmental impairment. For both of these studies, whether the anomalies would have been identified with a different aneuploidy screening methodology is not addressed. Citations #8 and #10 were published before the date of all 3 guidelines that informed this recommendation. The EbGS bases their

DRAFT

Stakeholder	#	Comment	Disposition
			guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions. EbGS does not see the need for a NT determination if an alternative screening method is chosen.
Carrier Screening			
C	20	Carrier screening: We would request that HERC consider the globalization of the population when making recommendations regarding carrier screening during pregnancy. Increasingly, parents report being of a mixed ethnic background and making screening determinations on this parameter alone is difficult. There is also emerging evidence that carrier frequencies in low risk populations may be higher than we would have thought. For instance, data from Counsyl indicate a high rate of carriers of traditional Ashkenazi Jewish conditions in individuals who do not report Jewish ancestry. 23 Due to these emerging trends, a carrier screening program will need to evolve to meet the needs of patients. Limiting screening based on ethnic background alone will increasingly miss at risk individuals. Guidelines based on general population data will likely be necessary to mirror the changes in ethnicity in the population.	Citation #23 is an analysis of the ethnicity of individuals who underwent routine carrier screening and had positive findings. The authors report that of the 23,453 individuals screened, 433 would not have been identified as disease carriers in accordance with conventional ethnicity-based screening paradigms. While EbGS acknowledges this trend, no specific changes to the guidance recommendations appear to be indicated.
Genetic Counseling			
D	21	**Prenatal Genetic Counseling—*Why it Matters*** All pregnant women can benefit from genetic counseling. While we appreciate the Health Evidence Review Commission's coverage guidance for genetic counseling prior to CVS, amniocentesis, microarray testing, Fragile X screening and Spinal Muscular Atrophy screening, **we implore them to *recommend genetic counseling for all pregnant women***. It is our opinion that the current recommendations will benefit only a select population of women having prenatal genetic screening and testing. We are concerned that genetic counseling services will not be available to	While evidence has not been presented supporting the utility of genetic counseling for all women, EbGS understands the importance of providing this service for the first and fourth bulleted examples. EbGS does not believe the 2nd and 3rd bullets are sufficient justification for this service.

Stakeholder	#	Comment	Disposition
		women who may fall outside of these specific guidelines, including: • Women with a family history of a chromosome abnormality or genetic disorder • Women with an abnormal finding on ultrasound or other increased risk for aneuploidy who are request more information but do not intend to pursue CVS or amniocentesis • Women whose prenatal care provider is unable to unwilling to explain the risks, benefits and limitations of noninvasive prenatal screening options • Women who have been found to be a carrier for genetic conditions, such as CF, who desire further explanation and partner testing	
D	22	The American College of Obstetrics & Gynecology has recommended that all pregnant women be offered screening for genetic conditions including Down syndrome and cystic fibrosis (CF). Although obstetricians, midwives and family medicine physicians are expected to be the educated about genetic testing options in pregnancy, the complexity and number of screening options continue to evolve at a rapid pace.	EbGS does not disagree with these statements.
D	23	A 2009 ACOG survey found that almost half of Obstetricians felt their training was inadequate to counsel patients about first trimester screening options and only 31% of those surveyed had actually read the 2007 ACOG committee opinion regarding prenatal screening recommendations (Driscoll, et al. Screening for Down syndrome: Changing practice of Obstetricians. *American Journal of Obstetrics & Gynecology*, 2009; 200: 459).	Driscoll 2009 is a survey of ACOG members. With regard to the first statement, 40% of respondents felt that their training was less than adequate to counsel patients about 1st trimester options. However, 98% stated that they were either somewhat or well qualified to counsel patients about Down's syndrome screening, presumably due to ongoing education.
D	24	Studies in the literature have stated that the information about genetic testing provided in the first prenatal visit is inadequate for ensuring informed autonomous decision-making (Bernhardt et al. Prenatal Genetic Testing: Content of Discussion between Obstetric Providers and Pregnant Women. *Obstetrics & Gynecology*, 1998: 91:648). The authors of such studies implore physicians to improve their practice with the help of genetic counselors. Prenatal genetic counselors are specifically trained to work with couples pre-conceptually and during the prenatal period to: • *Provide risk assessment* • *Interpret family history, personal health history and genetic tests results*	Bernhardt 1998 is a case series of 169 pregnant patients whose first prenatal visit was evaluated for presence and content of genetic counseling. EbGS does not believe this is sufficient evidence of the need for formal genetic counseling in all women.

DRAFT

Stakeholder	#	Comment	Disposition
		• *Explain the risk, benefits and limitations of genetic screening and testing options* • *Provide education & supportive counseling* • *Ensure informed consent and patient autonomy*	
D	25	**Providing prenatal genetic counseling services to all pregnant women will improve the quality of care.** Genetic information and available genetic tests are expanding rapidly. Most physicians and nurses simply don't have the time to keep up with these changes.	Evidence of the need for genetic counseling in all women is lacking.
D	26	**Providing prenatal genetic counseling services to call pregnant women will save money** by avoiding inappropriate genetic tests, arranging for the tests that are both appropriate and economical, and by identifying people who do not need expensive screenings or treatments.	See comment #23.
C	27	Genetic Counseling: We agree with indications for genetic counseling approved by HERC, but feel that they may not be sufficient. One purpose of genetic counseling is to educate patients about testing options. Limiting genetic counseling as proposed jeopardizes patient care in limiting their access to quality information and jeopardizes coverage of the service if they opt for screening instead of diagnostic testing after genetic counseling. We would encourage a broader coverage of genetic counseling service to include pre-test counseling for aneuploidy screening (either in group or individual format). We believe that it is a useful service and is cost effective in helping to tailor testing based on parent's choices.24-25 In addition to the proposed guidelines, we request that post-test genetic counseling be covered in the event of a positive test result initiated through a genetic counseling process.	Citation #24 is a case series of 139 women that utilized a questionnaire to assess the decision-making process of pregnant women offered first trimester aneuploidy screening. Unclear how this study supports the need for genetic counseling for all women. Citation #25 is a review and discussion article. EbGS does not believe the evidence supports genetic counseling for all women.

DRAFT

References Provided by Commenters

A	None submitted
B	References embedded in comments
C	References: 1 Pandya, PP, Kondylios A, Hilbert L, et al: Chromosomal defects and outcome in 1015 fetuses with increased nuchal translucency. Ultrasound Obstet Gynecol 1995;5:15-9. 2 Wapner R, Thom E, Simpson JL, et al. First-trimester screening for trisomies 21 and 18. N Engl J Med 2003;349:1405-1413. 3 Malone FD, Canick JA, Ball RH, et al. First-trimester or second-trimester screening, or both, for Down's syndrome. N Engl J Med 2005;353:2001-2011. 4 Wald NJ, Rodeck C, Hackshaw AK, et al. First and second trimester antenatal screening for Down's syndrome: The results of the Serum, Urine and Ultrasound Screening Study (SURUSS). J Med Screen. 2003;10:56-104. 5 Jenkins TM, Waper RJ. Integrated screening for Down's syndrome. N Engl J Med 1999;341:1935. 6 Nicholaides KH, Spencer K, Avgidou K et al. Multicenter study of first-trimester screening for trisomy 21 in 75821 pregnancies: Results and estimation of the potential impact of individual risk orientated two-stage first trimester screening. Ultrasound Obstet Gynecol 2005; 25:221-226. 7 Ayras O, Tikkanen M, Eronen M, et al. Increased nuchal translucency and pregnancy outcome: a retrospective study of 1063 consecutive singleton pregnancies in a single referral institution. Prenatal Diagnosis 2013;33: 1. 8 Souka AP, von Kaisenberg CS, Hyett JA, et al. Increased nuchal translucency with normal karyotype. Am J Obstet Gynecol 2005;192:1005. 9 Mula R, Gonce A, Bennasar M, et al. Increased Nuchal Translucency and Normal Karyotype: Perinatal and Pediatric Outcomes at 2 Years of Age. Ultrasound Obstet Gynecol 2012;39:34. 10 Werner EF, Pastore LM, Karns LB, et al. Patient preferences for screening in the first trimester. Prenat Diagn 2008;28:1521. 11 Walsh JM and Goldberg JD. Fetal aneuploidy by maternal plasma DNA sequencing: a technology assessment. Prenat Diagn 2013;33:514. 12 Ashoor G, Syngelaki A, Wagner M, et al. Chromosome-selective sequencing of maternal plasma cell-free DNA for first trimester detection of trisomy 21 and trisomy 18. Am J Obstet Gynecol 2012; 206:322.e1-5 13 Ehrich M, Deciu C, Zweifelhofer T, et al. Noninvasive detection of fetal trisomy 21 by sequencing of DNA in maternal blood: a study in a clinical setting. Am J Obstet Gynecol 2011;204:205.e1-11. 14 Non-Invasive Prenatal Testing (NIPT) Factsheet. NCHPEG+NSGC 2012. 15 Noninvasive prenatal testing for fetal aneuploidy. Committee Opinion No. 545. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012;120:1532-4. 16 Position statement from the Aneuploidy Screening Committee on behalf of the board of the International Society for Prenatal Diagnosis. International Society for Prenatal Diagnosis. April 2013. 17 Gregg A, Gross S, Best R et al. ACMG statement on noninvasive prenatal screening for fetal aneuploidy. Genet Med 2013;15:395-8. 18 Sehnert AJ, Rhees B, Comstock D, et al. Optimal Detection of Fetal Chromosomal Abnormalities by Massively Parallel DNA Sequencing of Cell-Free Fetal DNA from Maternal Blood. Clinical Chemistry 2011;57:1042. 19 Skirton H and Patch C. Factors affecting the clinical use of non-invasive prenatal testing: a mixed methods systematic review. Prenatal Diagnosis 2013;33:532. 20 Hill M, Fisher J, Chitty LS, and Morris S. Women's and health professionals' preferences for prenatal tests for Down syndrome: a discrete choice experiment to contrast noninvasive prenatal diagnosis with current invasive tests. Genet Med 2012;14:905.

DRAFT

	21 Norton ME, Rose NC, and Benn P. Noninvasive Prenatal Testing for Fetal Aneuploidy: Clinical Assessment and a Plea for Restraint. Obstet Gynecol 2013;121:847. 22 Allyse MA, Sayres LC, Havard,M, et al. Best ethical practices for clinicians and laboratories in the provision of noninvasive prenatal testing. Prenatal Diagnosis 2013, 33, 1–6. 23 Lazarin G, Haque I, Nazareth S et al. An empirical estimate of carrier frequencies for 400+ casual Mendelian variants: results from an ethnically diverse clinical sample of 23453 individuals. Genet Med 2013;15:178-186. 24 Farrell RM, Nutter B, and Agatisa PK. Meeting patients' education and decision-making needs for first trimester prenatal aneuploidy screening. Prenat Diagn 2011;31:1222. 25 Pergament E, and Pergament D. Reproductive decisions after fetal genetic counseling. Best Practice & Research Clinical Obstetrics and Gynaecology 2012;26:517.
D	References embedded in comments
E	Song et al. Clinical utility and cost of non-invasive prenatal testing with cfDNA analysis in high-risk women based on a US population. *The Journal of Maternal-Fetal & Neonatal Medicine*, 2013. Ohno, M., & Caughey, A. The role of noninvasive prenatal testing as a diagnostic versus a screening tool- a cost-effectiveness analysis. *Prenatal Diagnosis*, 2013, 33, 1-6.

DRAFT