

Chromosomal Microarray Testing For Developmental Disorders (Prenatal and Postnatal)

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Introduction

Chromosomal microarray (CMA) testing for developmental disorders in the prenatal or postnatal setting is addressed by this guideline.

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

Procedures addressed by this guideline	Procedure codes
Chromosomal microarray [BAC], constitutional	81228
Chromosomal microarray [CGH], constitutional	S3870
Chromosomal microarray [SNP], constitutional	81229
Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and loss-of-heterozygosity variants, low-pass sequencing analysis	81349

Criteria

Introduction

Requests for chromosomal microarray (CMA) testing for developmental disorders in the prenatal and postnatal setting are reviewed using the following criteria.

Criteria

- Genetic Counseling:

- Pre- and post-test genetic counseling by an appropriate provider (as deemed by the Health Plan policy), AND
- Diagnostic Testing for Symptomatic Individuals:
 - No previous CMA testing,* and
 - Testing performed on living child or adult, and
 - Diagnosis cannot be made on clinical evaluation alone, and
 - A more appropriate targeted test is not available (e.g., chromosome analysis, fluorescence in situ hybridization [FISH], single gene sequencing, etc.), and
 - Common aneuploidy (trisomy 13, 18, 21, or sex chromosome) is not a suspected diagnosis, and
 - One of the following presentations:
 - Developmental delay/intellectual disability (DD/ID), or
 - Autism spectrum disorder, or
 - Major congenital cardiac anomaly[†], or
 - Multiple congenital anomalies[†], OR
- Diagnostic Testing for Intrauterine Fetal Demise or Stillbirth:
 - No previous CMA testing in the same pregnancy, and
 - A more appropriate targeted test is not available (e.g., chromosome analysis, FISH, single gene sequencing, etc.), and
 - Common aneuploidy (trisomy 13, 18, 21, or sex chromosome) is not a suspected diagnosis, and
 - One of the following presentations:
 - Major congenital cardiac anomaly[†], or
 - Multiple congenital anomalies[†], or
 - Fetal demise or stillbirth occurred at 20 weeks of gestation or later, OR
- Diagnostic Prenatal Testing:
 - No previous CMA testing in the same pregnancy, and
 - The member has sufficient risk of fetal copy number variant (CNV) to justify invasive prenatal diagnosis. [It is important to note that invasive diagnostic procedures such as chorionic villus sampling and amniocentesis are associated with risks; the provider and member must have determined that the associated benefits outweigh the risks.], AND
- Rendering laboratory is a qualified provider of service per the Health Plan policy

*Microarray is considered a first-tier test in the evaluation of postnatal developmental disorders. Therefore, it often is not necessary to do chromosome analysis or FISH in conjunction with microarray. Microarray requests following such testing will require review.

†**Multiple congenital anomalies** defined as 1) two or more major anomalies affecting different organ systems or 2) one major and two or more minor anomalies affecting different organ systems. **Major structural abnormalities** are generally serious enough as to require medical treatment on their own (such as surgery) and are not minor developmental variations that may or may not suggest an underlying disorder.

Chromosomal Microarray (CMA) Exclusions and Considerations

If routine karyotype and CMA are ordered simultaneously, only the most appropriate test based on clinical history will be considered for coverage. If CMA has been performed, the following tests are often excessive and thus not considered medically necessary. Each test may require medical necessity review.

- Routine karyotype: Full karyotype in addition to CMA is typically considered excessive. However, a limited 5 cell analysis may be approved in addition to CMA if criteria for CMA are met. This approval may be subject to claims review to ensure that the appropriate procedure code for a limited 5 cell analysis is billed (CPT 88261 x1, 88230 x1, 88291 x1).
- FISH Analysis
- Telomere Analysis
- More than one type of microarray analysis (i.e. if 81228 performed, 81229 is not medically necessary)
- CMA is not considered medically necessary in cases of family history of chromosome rearrangement in phenotypically normal individuals.
- CMA is not considered medically necessary in individuals experiencing infertility, structurally normal pregnancy losses that occur at less than 20 weeks, or recurrent pregnancy loss.
- When a multigene deletion/duplication panel is being requested and billed using a microarray procedure code (typically 81228 or 81229), please refer to the *Genetic Testing by Multigene Panels* clinical use guideline; do not apply the criteria in this guideline.
- CMA for delineation of deletion, duplication, or translocation breakpoints will be reviewed on a case by case basis.
- CMA for determination of whether a translocation is balanced or unbalanced will be reviewed on a case by case basis.

Billing and Reimbursement

Introduction

This section outlines the billing requirements for tests addressed in this guideline. These requirements will be enforced during the case review process whenever appropriate. Examples of requirements may include specific coding scenarios, limits on allowable test combinations or frequency and/or information that must be provided on a claim for automated processing. Any claims submitted without the necessary information to allow for automated processing (e.g. ICD code, place of service, etc.) will not be reimbursable as billed. Any claim may require submission of medical records for post service review.

- CMA is only reimbursable once per lifetime.
- When CMA is otherwise reimbursable, the following limitations apply:
 - Only one type of microarray analysis (e.g., 81228, 81229 or 81349) will be reimbursed.
 - A limited 5 cell chromosome analysis (88261x1, 88230x1, 88291x1) may be reimbursed in addition to the CMA.
 - FISH or other procedure codes that do not accurately describe the test methodology performed (e.g. 88271) are not eligible for reimbursement of CMA.
- If CMA has been performed, the following tests are not reimbursable:
 - Routine karyotype
 - FISH Analysis
 - Telomere Analysis

What are Copy Number Variants in Developmental Disorders?

Introduction

Copy number variation is when the number of copies of genetic material differs between individuals. When present, the following developmental disorders often prompt an evaluation for copy number variants: intellectual disability (ID), global developmental delay (GDD), autism spectrum disorders (ASD), and congenital anomalies.

Copy Number Variants (CNVs)

Copy number variants (CNVs) are deletions and duplications of genetic material. CNVs account for a significant proportion of congenital anomalies and developmental disorders without a clear etiology based on clinical findings. CNVs are detected using

chromosomal microarray (CMA) testing. CMA is known by several names including array-comparative genomic hybridization (aCGH) and single-nucleotide polymorphism arrays (SNP-array).

Incidence

ID and congenital anomalies affect approximately 3-4% of the general population.¹ The incidence of GDD is comparable to ID. ASD, which now includes autistic disorder, pervasive developmental disorder not otherwise specified (PDD-NOS), and Asperger syndrome, are also of increasing concern, with recent CDC incidence figures estimating 1 in 36 affected children.²

Heart defects are the most common congenital anomaly, affecting nearly 1-1.2% of live births.³ Sixty to eighty percent of major structural anomalies are identified prenatally by ultrasound evaluation.⁴

Cause

The etiology of developmental disorders and congenital anomalies is complex. Some developmental problems may be caused by non-genetic factors, such as injury, birth complications, endocrine disorders, toxic exposures, and infection. However, genetic causes also play a significant role.⁵⁻⁸

A clinical genetics evaluation can identify a cause in a portion of individuals with ID, GDD, or ASD. Identifying an underlying genetic cause in these individuals may:⁵⁻⁸

- Provide diagnostic and prognostic information
- Improve health screening and prevention for some conditions
- Allow for testing of family members and accurate recurrence risk counseling, and
- Empower the individual and family to acquire needed services and support

CMA on chorionic villi or amniocytes is indicated in any pregnancy in which diagnostic testing for chromosome abnormalities and CNVs is desired.⁹⁻¹¹ Identifying an underlying genetic cause in these individuals may:⁶

- Provide diagnostic and prognostic information
- Guide prenatal management and decision-making, and
- Allow for testing of family members and accurate recurrence risk counseling.

Parental Testing

If a CNV is detected in a child, it may be helpful to test both parents to determine whether the CNV is inherited or a new (de novo) genetic change. This information along with parental findings can be used to weigh the possibilities of a benign vs. pathogenic variant. However, even with parental studies, the clinical outcome may remain unclear.^{1,9} A de novo variant is more likely to represent a pathologic abnormality.¹

Clinical Classification of CNVs

In a joint consensus recommendation, the American College of Medical Genetics and Genomics (ACMG) and the Clinical Genome resource (ClinGen) introduced updated standards to help reduce discordance in clinical classifications of CNVs, including those detected during postnatal or prenatal testing.^{12,13} The standards include a semi-quantitative point-based scoring system metric for CNV classification, including separate scoring metrics for copy number losses and copy number gains. Evaluation of the inheritance pattern, including whether the CNV is inherited or a new (de novo) genetic change, factors into this scoring system.

Test information

Introduction

Testing for developmental disorders in the prenatal and postnatal setting may include CMA testing.

Chromosomal Microarray

CMA testing generally works by fluorescently tagging DNA from an individual's test sample with one color and combining it with a control sample tagged in a different color. The two samples are mixed and then added to the array chip, where they compete to hybridize with the DNA fragments on the chip. By comparing the test sample versus the control, computer analysis can determine where genetic material has been deleted or duplicated in the individual.

There are a growing number of CMA testing platforms, including non-chip based applications, which differ in approach and resolution. Clinical laboratories may not only differ in the arrays that they utilize but also in their reporting practices. Although testing guidelines do not endorse one CMA over another, it is typically advisable that coverage of an ordered CMA is better than that offered by a standard karyotype and that the minimum resolution of the CMA provided by the laboratory is adequate. The inclusion of analysis of subtelomeric regions and known microdeletion syndromes with CMA testing obviates the need for additional FISH analysis.

CMA testing offers advantages over conventional karyotyping with regard to resolution and yield. However, there are some limitations of CMA testing including:

- the inability to detect
 - balanced chromosomal rearrangements such as translocations or inversions
 - certain forms of polyploidy
 - sex chromosome aneuploidy dependent on the gender control used
 - low level mosaicism
 - some marker chromosomes

- the detection of CNVs of uncertain clinical significance
- the inability to differentiate free trisomies from unbalanced Robertsonian translocations.

Diagnostic Yield

Diagnostic yield for CMA differs based on clinical presentation.

The diagnostic yield for CMA across various prenatal clinical settings is presented below.

- The results of one multicenter trial of CMA in the prenatal setting reported that CMA identified a clinically relevant deletion or duplication in 6% of prenatal cases with a structural anomaly and normal karyotype. In addition, 1.7% of prenatal cases with an indication of advanced maternal age or positive screening results and normal karyotype had a clinically relevant deletion or duplication identified by CMA.¹⁰
- In a large series of fetuses with ultrasound anomalies and normal conventional karyotype, CMA detected chromosome abnormalities in 5% of fetuses and up to 10% in those with 3 or more anatomic abnormalities.¹⁴
- A cohort study utilizing amniocentesis samples reported karyotype detected abnormalities in 5.41% of fetuses and CMA detected abnormalities in 9.14% of fetuses. The detection rate of CMA combined with karyotype was 0.35% higher than CMA alone and 4.08% higher than karyotype alone.¹⁵
- A retrospective study of 523 prenatal (amniocentesis) and 319 products-of-conception cases with a wide variety of referral indications demonstrated a diagnostic yield of clinically significant CMA findings in 7.8% and 16.3% of cases, respectively.¹⁶
- Another study showed an approximate 55% diagnostic yield when performing CMA in first trimester losses.^{17,18}
- CMA had a diagnostic yield of "41.9% in all stillbirths, 34.5% in antepartum stillbirths, and 53.8% in stillbirths with anomalies."^{19,20}
- A meta-analysis of fetuses with congenital heart disease (CHD) found a pooled proportion of overall chromosomal abnormalities, aneuploidy, 22q11.2 deletion, and other CNVs was 23%, 19%, 2%, and 4%, respectively.²¹ In a later study of fetuses with severe CHD and absence of aneuploidy, a CNV was identified in 9.9% of cases.²²
- CMA may also be useful in the workup of non-immune fetal hydrops and fetal ventriculomegaly.²³⁻²⁵

Some forms of mosaic aneuploidy will only be detected by a cultured sample, as typically required for karyotype and would not be observed using CMA on a direct sample.²⁶

The diagnostic yield for CMA across various postnatal clinical settings is presented below.

- Approximately 10-19% of people with unexplained ID or developmental delay (DD) will have CNVs.^{1,7,8,27}
- CMA finds a pathogenic CNV in 5% to 14% of those with ASD who are tested clinically by this method.²⁸
- The diagnostic yield in individuals with ASD is higher in those with a syndromic presentation, meaning that they have additional findings.⁵

Guidelines and evidence

American Academy of Pediatrics

The American Academy of Pediatrics (AAP, 2014; reaffirmed 2019) Committee on Genetics recommended genetics evaluation for all individuals following the diagnosis of GDD or ID. They stated:²⁹

"[i]f diagnosis is unknown and no clinical diagnosis is strongly suspected, begin the stepwise evaluation process:

- Chromosomal microarray should be performed in all.
- Specific metabolic testing should be considered and should include serum total homocysteine, acyl-carnitine profile, amino acids; and urine organic acids, glycosaminoglycans, oligosaccharides, purines, pyrimidines, GAA/creatine metabolites.
- Fragile X genetic testing should be performed in all."

American College of Medical Genetics and Genomics

The American College of Medical Genetics and Genomics (ACMG, 2010; reaffirmed 2020) Professional Practice and Guidelines Committee recommended CMA as a first-tier test for the evaluation of individuals who have the following:^{6,7}

- "Multiple anomalies not specific to a well-delineated genetic syndrome."
- "Apparently non-syndromic DD [developmental delay]/ID [intellectual disability]."
- "Autism spectrum disorders"

American College of Obstetricians and Gynecologists and Society for Maternal Fetal Medicine

The American College of Obstetricians and Gynecologists (ACOG, 2016; reaffirmed 2023) and Society for Maternal Fetal Medicine (SMFM, 2016; reaffirmed 2023) joint committee opinion on chromosomal microarray stated:³⁰

- "Chromosomal microarray analysis of fetal tissue (i.e. amniotic fluid, placenta, or products of conception) is recommended in the evaluation of intrauterine death or

stillbirth when further cytogenetic analysis is desired because of the test's increased likelihood of obtaining results and improved detection of causative abnormalities."

- "Additional information is needed regarding the clinical use and cost-effectiveness in cases of recurrent miscarriage and structurally normal pregnancy losses at less than 20 weeks of gestation."
- "The routine use of whole-genome or whole-exome sequencing for prenatal diagnosis is not recommended outside of the context of clinical trials until sufficient peer-reviewed data and validation studies are published."
- "Prenatal chromosomal microarray analysis is recommended for a patient with a fetus with one or more major structural abnormalities identified on ultrasonographic examination and who is undergoing invasive prenatal diagnosis. This test typically can replace the need for fetal karyotype."
- "In a patient with a structurally normal fetus who is undergoing invasive prenatal diagnostic testing, either fetal karyotyping or chromosomal microarray analysis can be performed."

The American College of Obstetricians and Gynecologists (ACOG, 2016) and Society for Maternal Fetal Medicine (SMFM, 2016) practice bulletin on prenatal diagnostic testing stated:³¹

- CMA is recommended "as the primary test (replacing conventional karyotype) for patients undergoing prenatal diagnosis for the indication of a fetal structural abnormality detected by ultrasound examination."
- "It is recommended that chromosomal microarray analysis be made available to any patient choosing to undergo invasive diagnostic testing."

In a joint Obstetric Care Consensus statement, the American College of Obstetricians and Gynecologists (ACOG, 2020) and Society for Maternal Fetal Medicine (SMFM, 2020) stated the following:³²

- "We recommend that prenatal genetic screening (serum screening with or without nuchal translucency ultrasonography or cell-free DNA screening) and diagnostic testing (chorionic villus sampling or amniocentesis) options be discussed and offered to all pregnant individuals regardless of age or risk of chromosomal abnormality. After review and discussion, every patient has the right to pursue or decline prenatal genetic screening and diagnostic testing. (GRADE 1A. Strong recommendation, high-quality evidence.)"

European Heart Rhythm Association, Heart Rhythm Society, Asia Pacific Heart Rhythm Society, and Latin American Heart Rhythm Society

The European Heart Rhythm Association, Heart Rhythm Society, Asia Pacific Heart Rhythm Society, and Latin American Heart Rhythm Society (EHRA/HRS/APHRS/LAHRs, 2022) issued consensus statements regarding genetic testing for cardiac conditions.³³ The consensus statements were categorized as follows:

- Supported by strong observational evidence and author's consensus
- Some evidence and general agreement favor the usefulness/ efficacy of a test
- There is evidence or general agreement not to recommend a test

The following recommendations were made for chromosomal microarray:³³

- Regarding antenatal testing: "When foetal congenital heart disease (CHD) is identified on antenatal ultrasound examinations, a chromosomal microarray (CMA) or CNV sequencing (CNV seq) of foetal tissue [amniocentesis or chorionic villous sample (CVS)] should be offered." [Supported by strong observational evidence and author's consensus]
- Regarding neonates and infants requiring investigation or procedures for complex CHD: "CMA or CNV seq is indicated in infants with CHD to identify pathogenic CNVs." [Supported by strong observational evidence and author's consensus]
- Regarding individuals with CHD and extracardiac anomalies: "CMA or CNV seq is indicated in patients with CHD and extracardiac anomalies to identify pathogenic CNVs." [Supported by strong observational evidence and author's consensus]
- Regarding sporadic non-syndromic CHD (excluding neonates or infants): "CMA or CNV seq for pathogenic CNVs may be performed in older individuals with sporadic non-syndromic CHD." [Some evidence and general agreement favor the usefulness/ efficacy of a test]

International Standard Cytogenomic Array Consortium

The International Standard Cytogenomic Array Consortium (ISCA, 2010) recommended offering CMA as a first-tier genetic test, in place of karyotype, for individuals with unexplained developmental delay/intellectual disability, autism spectrum disorders, or birth defects.¹

Society for Maternal Fetal Medicine

The Society for Maternal Fetal Medicine (SMFM, 2016) published a consult series that stated:³⁴

- We recommend that CMA "be offered when genetic analysis is performed in cases with fetal structural anomalies and/or stillbirth and replaces the need for fetal karyotype in these cases." (GRADE 1A).

Note This benefit/harm statement only applies to those jurisdictions that do not have Medicare guidance. Based upon the guidelines and evidence provided in the clinical policy, following EviCore's criteria for chromosomal microarray testing for developmental disorders (prenatal and postnatal) will ensure that testing will be available to those members most likely to benefit from a genetic diagnosis. For those not meeting criteria, it ensures alternate diagnostic strategies are considered.

However, it is possible that some members who would benefit from the testing, but do not meet criteria, will not receive an immediate approval for testing.

References

1. Miller DT, Adam MP, Aradhya S, et al. Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies. *Am J Hum Genet.* 2010;86(5):749-764.
2. Autism Spectrum Disorder (ASD), Centers for Disease Control and Prevention. Last reviewed April 4, 2023. <https://www.cdc.gov/ncbddd/autism/data.html>
3. Pierpont ME, Brueckner M, Chung WK, et al. Genetic basis for congenital heart disease: Revisited: A scientific statement from the American Heart Association. *Circulation.* 2018;138(21):e653-e711. doi: 10.1161/cir.0000000000000606
4. Edwards L and Hui L. First and second trimester screening for fetal structural anomalies. *Semin Fetal Neonatal Med.* 2018 Apr;23(2):102-111.
5. Schaefer GB, Mendelsohn NJ. Professional Practice and Guidelines Committee. Clinical genetics evaluation in identifying the etiology of autism spectrum disorders: 2013 guideline revisions. *Genet Med.* 2013 May;15(5):399-407. doi: 10.1038/gim.2013.32.
6. Manning M, Hudgins L. Professional Practice and Guidelines Committee. American College of Medical Genetics Practice Guidelines: Array-based technology and recommendations for utilization in medical genetics practice for detection of chromosomal abnormalities. *Genet Med.* 2010 (Reaffirmed 2020);12(11):742-745.
7. Manning M, Hudgins L. Professional Practice and Guidelines Committee. American College of Medical Genetics Clinical Practice Resource (Addendum to 2010): Array-based technology and recommendations for utilization in medical genetics practice for detection of chromosomal abnormalities. *Genet Med.* 2020;22:2126.
8. Sagoo GS, Butterworth AS, Sanderson S, Shaw-Smith C, Higgins JP, Burton H. Array CGH in patients with learning disability (mental retardation) and congenital anomalies: updated systematic review and meta-analysis of 19 studies and 13,926 subjects. *Genet Med.* 2009 Mar;11(3):139-46.
9. American College of Obstetricians and Gynecologists and Society for Maternal Fetal Medicine Practice Bulletin Number 162: Prenatal diagnostic testing for genetic disorders. *Obstet Gynecol.* 2016 May;127(5):e108-22.
10. Wapner RJ, Martin CI, Levy B, et al. Chromosomal microarray versus karyotyping for prenatal diagnosis. *N Engl J Med.* 2012 Dec;367(23):2175-84.

11. Hay SB, Sahoo T, Travis MK, et al. ACOG and SMFM guidelines for prenatal diagnosis; Is karyotyping really sufficient? *Prenat Diagn*. 2018 Feb; 38(3):184-89.
12. Riggs ER, Andersen EF, Cherry AM, et al. Technical standards for the interpretation and reporting of constitutional copy-number variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics (ACMG) and the Clinical Genome Resource (ClinGen) *Genet Med*. 2020;22(2):245-257. doi:10.1038/s41436-019-0686-8.
13. Riggs ER, Andersen EF, Cherry AM, et al. Correction: Technical standards for the interpretation and reporting of constitutional copy-number variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics (ACMG) and the Clinical Genome Resource (ClinGen). *Genet Med*. 2021;23(11):2230. doi: 10.1038/s41436-021-01150-9
14. Hillman SC, Pretlove S, Coomarasamy A, et al. Additional information from array comparative genomic hybridization technology over conventional karyotyping in prenatal diagnosis: a systemic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2011 Jan;37(1):6-14.
15. Wang J, Wang D, Yin Y, et al. Assessment of combined karyotype analysis and chromosome microarray analysis in prenatal diagnosis: a cohort study of 3710 pregnancies. *Genet Res (Camb)*. 2022 Dec 29;2022:6791439. doi: 10.1155/2022/6791439
16. Olayiwola JO, Marhabaie M, Koboldt D, et al. Clinically significant findings in a decade-long retrospective study of prenatal chromosomal microarray testing. *Mol Genet Genomic Med*. 2024;12(3):e2349. doi: 10.1002/mgg3.2349
17. Pauta M, Grande M, Rodriguez-Revenga L, Kolomietz E, Borrell A. Added value of chromosomal microarray analysis over karyotyping in early pregnancy loss: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2018;51(4):453-462.
18. Wang Y, Cheng Q, Meng L, et al. Clinical application of SNP array analysis in first-trimester pregnancy loss: a prospective study. *Clin Genet*. 2016;91(6):849-858.
19. Management of Stillbirth: Obstetric Care Consensus no. 10. *Obstet Gynecol*. 2020 (Reaffirmed 2021);135(3):e110-e132. doi:10.1097/AOG.0000000000003719
20. Obstetric Care Consensus No. 10: Management of Stillbirth: Correction. *Obstet Gynecol*. 2023;141(5):1030. doi: 10.1097/aog.0000000000005178

21. Wang H, Lin X, Lyu G, et al. Chromosomal abnormalities in fetuses with congenital heart disease: a meta-analysis. *Arch Gynecol Obstet*. 2023;308(3):797-811. doi: 10.1007/s00404-023-06910-3
22. van Nisselrooij AEL, Lugthart MA, Clur SA, et al. The prevalence of genetic diagnoses in fetuses with severe congenital heart defects. *Genet Med*. 2020;22(7):1206-1214. doi: 10.1038/s41436-020-0791-8
23. Society of Obstetricians and Gynecologists of Canada: Investigation and management of non-immune fetal hydrops. *J Obstet Gynaecol Can*. 2013 Oct;35(10):923-38.
24. Norton ME, Chauhan SP, Dashe JS, Society for Maternal-Fetal Medicine (SMFM). Society for Maternal-Fetal Medicine (SMFM) Clinical Guideline #7: nonimmune hydrops fetalis. *Am J Obstet Gynecol*. 2015;212(2):127-139.
25. Society for Maternal-Fetal Medicine (SMFM), Fox NS, Monteagudo A, et al. Mild fetal ventriculomegaly: diagnosis, evaluation, and management. *Am J Obstet Gynecol*. 2018;219(1):B2-B9. doi: 10.1016/j.ajog.2018.04.039
26. Hao M, Li L, Zhang H, et al. The difference between karyotype analysis and chromosome microarray for mosaicism of aneuploid chromosomes in prenatal diagnosis. *J Clin Lab Anal*. 2020; 34:e23514. doi:10.1002/jcla.23514
27. Hochstenbach R, van Binsbergen E, Engelen J, et al. Array analysis and karyotyping: workflow consequences based on a retrospective study of 36,325 patients with idiopathic developmental delay in the Netherlands. *Eur J Med Genet*. 2009 Jul-Aug;52(4):161-9.
28. Hyman SL, Levy SE, Myers SM; Council on Children with Disabilities, Section on Developmental and Behavioral Pediatrics. Identification, Evaluation, and Management of Children With Autism Spectrum Disorder. *Pediatrics*. 2020 Jan;145(1):e20193447. doi: 10.1542/peds.2019-3447.
29. Moeschler JB, Shevell M, Committee on Genetics. Comprehensive evaluation of the child with intellectual disability or global developmental delays. *Pediatrics*. 2014 (Reaffirmed 2019);134(3):e903-18.
30. American College of Obstetricians and Gynecologists and Society for Maternal Fetal Medicine Committee Opinion No. 682. Microarrays and next-generation sequencing technology: The use of advanced genetic diagnostic tools in obstetrics and gynecology. *Obstet Gynecol*. 2016 (Reaffirmed 2023);128:e262–8.
31. American College of Obstetricians and Society for Maternal-Fetal Medicine Practice Bulletin Number 162: Prenatal Diagnostic Testing for Genetic Disorders. *Obstet Gynecol*. 2016 May;127(5):e108-22.

32. American College of Obstetricians and Gynecologists' Committee on Clinical Consensus-Obstetrics, Gantt A, Metz TD, et al. Obstetric Care Consensus #11, Pregnancy at age 35 years or older. *Am J Obstet Gynecol*. 2023;228(3):B25-B40. doi: 10.1016/j.ajog.2022.07.022
33. Wilde AAM, Semsarian C, Márquez MF, et al. European Heart Rhythm Association (EHRA)/Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) Expert Consensus Statement on the state of genetic testing for cardiac diseases. *Europace*. 2022;euac030. doi:10.1093/europace/030.
34. Society for Maternal Fetal Medicine, Dugoff L, Norton ME, Kuller JA. The use of chromosomal microarray for prenatal diagnosis. *Am J Obstet Gynecol*. 2016;215(4):B2-B9.