Chromosome Microarray Testing (Non-Oncology Conditions) (for Idaho Only)

Policy Number: CS017ID.D
Effective Date: June 1, 2026

➲ Instructions for Use

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- Preimplantation Genetic Testing and Related Services (for Idaho Only)
- Whole Exome and Whole Genome Sequencing (Non-Oncology Conditions) (for Idaho Only)

Application

This Medical Policy only applies to the state of Idaho, including Idaho Medicaid Plus plans.

Coverage Rationale

State-Specific Criteria

For medical necessity clinical coverage criteria for genetic testing, refer to the Idaho Medicaid Provider Handbook, Provider Guidelines, Laboratory Services: Genetic Testing.

Non–State-Specific Criteria

Chromosome microarray testing using array comparative genomic hybridization (aCGH) and/or single-nucleotide polymorphism (SNP) array is proven and medically necessary for the following:

- Evaluation of an embryo/fetus in individuals undergoing invasive prenatal testing (i.e., amniocentesis, chorionic villus sampling, or fetal tissue sampling)
- Evaluation of individuals with one or more of the following:
  - Autism spectrum disorder (ASD)
  - Isolated severe congenital heart disease
  - Multiple anomalies that are not specific to a Well-Delineated Genetic Syndrome and cannot be identified by a clinical evaluation alone
  - Developmental Delay/Intellectual Disability where a specific syndrome is not suspected

Chromosome microarray testing using aCGH or SNP array is unproven and not medically necessary for all other populations and conditions due to insufficient evidence of efficacy.

Note: Preimplantation genetic testing (PGT) is addressed in the Medical Policy titled Preimplantation Genetic Testing and Related Services (for Idaho Only).

Medical Records Documentation Used for Reviews

Benefit coverage for health services is determined by the federal, state, or contractual requirements, and applicable laws that may require coverage for a specific service. Medical records documentation may be required to assess whether the member meets the clinical criteria for coverage but does not guarantee coverage of the services requested.

The patient's medical record must contain documentation that fully supports the medical necessity for the requested services. This documentation includes, but is not limited to, relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures. Documentation supporting the medical necessity should be legible, maintained in the patient's medical record, and must be made available upon request.

Definitions

Developmental Delay: Developmental Delay may be used to describe children younger than 5 years of age who present with delays in the attainment of developmental milestones at the expected age (Moeschler and Shevell, 2014; reaffirmed 2019).

Intellectual Disability: A condition diagnosed before age 18 that includes below-average intellectual function and a lack of skills necessary for daily living (MedlinePlus, 2020).

Intrauterine Fetal Demise or Stillbirth: Fetal death at or after 20 weeks gestation [American College of Obstetricians and Gynecologists (ACOG), Society of Maternal Fetal Medicine (SMFM), 2020; reaffirmed 2021].

Prenatal Diagnosis: A laboratory test performed on fetal deoxyribonucleic acid (DNA) or chromosomes before birth to determine if a fetus has a genetic or chromosomal disorder (ACOG, 2016a; reaffirmed 2023).

Well-Delineated Genetic Syndrome: A syndrome is a collection of recognizable traits or abnormalities that tend to occur together and are associated with a specific disease. Distinguishing characteristics, such as specific facial features or other physical traits, lab tests, or family history can be used to identify a genetic syndrome. (Talking Glossary of Genomic and Genetic Terms, National Human Genome Research Institute, 2024). Examples of Well-Delineated Genetic Syndromes include, but are not limited to: Down syndrome, Klinefelter syndrome, Marfan syndrome, neurofibromatosis type 1, osteogenesis imperfecta, Prader-Willi syndrome, Rett syndrome, trisomy 13 (Patau syndrome), Trisomy 18 (Edwards syndrome), Turner syndrome, and Williams syndrome.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
0156U	Copy number (e.g., intellectual disability, dysmorphology), sequence analysis
0209U	Cytogenomic constitutional (genome-wide) analysis, interrogation of genomic regions for copy number, structural changes, and areas of homozygosity for chromosomal abnormalities
81228	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number variants, comparative genomic hybridization [CGH] microarray analysis
81229	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants, comparative genomic hybridization (CGH) microarray analysis
81349	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and loss-of-heterozygosity variants, low-pass sequencing analysis
81479	Unlisted molecular pathology procedure

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HCPCS Code	Description
S3870	Comparative genomic hybridization (CGH) microarray testing for developmental delay, autism spectrum disorder and/or intellectual disability

Diagnosis Code	Description
F70	Mild intellectual disabilities
F71	Moderate intellectual disabilities
F72	Severe intellectual disabilities
F73	Profound intellectual disabilities
F78.A1	SYNGAP1-related intellectual disability
F78.A9	Other genetic related intellectual disability
F79	Unspecified intellectual disabilities
F80.0	Phonological disorder
F80.1	Expressive language disorder
F80.2	Mixed receptive-expressive language disorder
F80.4	Speech and language development delay due to hearing loss
F80.81	Childhood onset fluency disorder
F80.82	Social pragmatic communication disorder
F80.89	Other developmental disorders of speech and language
F80.9	Developmental disorder of speech and language, unspecified
F81.0	Specific reading disorder
F81.2	Mathematics disorder
F81.81	Disorder of written expression
F81.89	Other developmental disorders of scholastic skills
F81.9	Developmental disorder of scholastic skills, unspecified
F82	Specific developmental disorder of motor function
F84.0	Autistic disorder
F84.3	Other childhood disintegrative disorder
F84.5	Asperger's syndrome
F84.8	Other pervasive developmental disorders
F84.9	Pervasive developmental disorder, unspecified
F88	Other disorders of psychological development
F89	Unspecified disorder of psychological development
H93.25	Central auditory processing disorder
N96	Recurrent pregnancy loss
O02.1	Missed abortion
O02.89	Other abnormal products of conception
O03.4	Incomplete spontaneous abortion without complication
O03.9	Complete or unspecified spontaneous abortion without complication
O09.511	Supervision of elderly primigravida, first trimester
O09.512	Supervision of elderly primigravida, second trimester
O09.513	Supervision of elderly primigravida, third trimester
O09.519	Supervision of elderly primigravida, unspecified trimester
O09.521	Supervision of elderly multigravida, first trimester
O09.522	Supervision of elderly multigravida, second trimester
O09.523	Supervision of elderly multigravida, third trimester
O09.529	Supervision of elderly multigravida, unspecified trimester

Diagnosis Code	Description
O26.20	Pregnancy care for patient with recurrent pregnancy loss, unspecified trimester
O26.21	Pregnancy care for patient with recurrent pregnancy loss, first trimester
O26.22	Pregnancy care for patient with recurrent pregnancy loss, second trimester
O26.23	Pregnancy care for patient with recurrent pregnancy loss, third trimester
O28.0	Abnormal hematological finding on antenatal screening of mother
O28.1	Abnormal biochemical finding on antenatal screening of mother
O28.2	Abnormal cytological finding on antenatal screening of mother
O28.3	Abnormal ultrasonic finding on antenatal screening of mother
O28.4	Abnormal radiological finding on antenatal screening of mother
O28.5	Abnormal chromosomal and genetic finding on antenatal screening of mother
O28.8	Other abnormal findings on antenatal screening of mother
O28.9	Unspecified abnormal findings on antenatal screening of mother
O35.00X0	Maternal care for (suspected) central nervous system malformation or damage in fetus, unspecified, not applicable, or unspecified
O35.00X1	Maternal care for (suspected) central nervous system malformation or damage in fetus, unspecified, fetus 1
O35.00X2	Maternal care for (suspected) central nervous system malformation or damage in fetus, unspecified, fetus 2
O35.00X3	Maternal care for (suspected) central nervous system malformation or damage in fetus, unspecified, fetus 3
O35.00X4	Maternal care for (suspected) central nervous system malformation or damage in fetus, unspecified, fetus 4
O35.00X5	Maternal care for (suspected) central nervous system malformation or damage in fetus, unspecified, fetus 5
O35.00X9	Maternal care for (suspected) central nervous system malformation or damage in fetus, unspecified, other fetus
O35.01X0	Maternal care for (suspected) central nervous system malformation or damage in fetus, agenesis of the corpus callosum, not applicable or unspecified
O35.01X1	Maternal care for (suspected) central nervous system malformation or damage in fetus, agenesis of the corpus callosum, fetus 1
O35.01X2	Maternal care for (suspected) central nervous system malformation or damage in fetus, agenesis of the corpus callosum, fetus 2
O35.01X3	Maternal care for (suspected) central nervous system malformation or damage in fetus, agenesis of the corpus callosum, fetus 3
O35.01X4	Maternal care for (suspected) central nervous system malformation or damage in fetus, agenesis of the corpus callosum, fetus 4
O35.01X5	Maternal care for (suspected) central nervous system malformation or damage in fetus, agenesis of the corpus callosum, fetus 5
O35.01X9	Maternal care for (suspected) central nervous system malformation or damage in fetus, agenesis of the corpus callosum, other fetus
O35.02X0	Maternal care for (suspected) central nervous system malformation or damage in fetus, anencephaly, not applicable or unspecified
O35.02X1	Maternal care for (suspected) central nervous system malformation or damage in fetus, anencephaly, fetus 1
O35.02X2	Maternal care for (suspected) central nervous system malformation or damage in fetus, anencephaly, fetus 2
O35.02X3	Maternal care for (suspected) central nervous system malformation or damage in fetus, anencephaly, fetus 3
O35.02X4	Maternal care for (suspected) central nervous system malformation or damage in fetus, anencephaly, fetus 4

Diagnosis Code	Description
O35.02X5	Maternal care for (suspected) central nervous system malformation or damage in fetus, anencephaly, fetus 5
O35.02X9	Maternal care for (suspected) central nervous system malformation or damage in fetus, anencephaly, other fetus
O35.03X0	Maternal care for (suspected) central nervous system malformation or damage in fetus, choroid plexus cysts, not applicable or unspecified
O35.03X1	Maternal care for (suspected) central nervous system malformation or damage in fetus, choroid plexus cysts, fetus 1
O35.03X2	Maternal care for (suspected) central nervous system malformation or damage in fetus, choroid plexus cysts, fetus 2
O35.03X3	Maternal care for (suspected) central nervous system malformation or damage in fetus, choroid plexus cysts, fetus 3
O35.03X4	Maternal care for (suspected) central nervous system malformation or damage in fetus, choroid plexus cysts, fetus 4
O35.03X5	Maternal care for (suspected) central nervous system malformation or damage in fetus, choroid plexus cysts, fetus 5
O35.03X9	Maternal care for (suspected) central nervous system malformation or damage in fetus, choroid plexus cysts, other fetus
O35.04X0	Maternal care for (suspected) central nervous system malformation or damage in fetus, encephalocele, not applicable or unspecified
O35.04X1	Maternal care for (suspected) central nervous system malformation or damage in fetus, encephalocele, fetus 1
O35.04X2	Maternal care for (suspected) central nervous system malformation or damage in fetus, encephalocele, fetus 2
O35.04X3	Maternal care for (suspected) central nervous system malformation or damage in fetus, encephalocele, fetus 3
O35.04X4	Maternal care for (suspected) central nervous system malformation or damage in fetus, encephalocele, fetus 4
O35.04X5	Maternal care for (suspected) central nervous system malformation or damage in fetus, encephalocele, fetus 5
O35.04X9	Maternal care for (suspected) central nervous system malformation or damage in fetus, encephalocele, other fetus
O35.05X0	Maternal care for (suspected) central nervous system malformation or damage in fetus, holoprosencephaly, not applicable, or unspecified
O35.05X1	Maternal care for (suspected) central nervous system malformation or damage in fetus, holoprosencephaly, fetus 1
O35.05X2	Maternal care for (suspected) central nervous system malformation or damage in fetus, holoprosencephaly, fetus 2
O35.05X3	Maternal care for (suspected) central nervous system malformation or damage in fetus, holoprosencephaly, fetus 3
O35.05X4	Maternal care for (suspected) central nervous system malformation or damage in fetus, holoprosencephaly, fetus 4
O35.05X5	Maternal care for (suspected) central nervous system malformation or damage in fetus, holoprosencephaly, fetus 5
O35.05X9	Maternal care for (suspected) central nervous system malformation or damage in fetus, holoprosencephaly, other fetus
O35.06X0	Maternal care for (suspected) central nervous system malformation or damage in fetus, hydrocephaly, not applicable or unspecified
O35.06X1	Maternal care for (suspected) central nervous system malformation or damage in fetus, hydrocephaly, fetus 1

Diagnosis Code	Description
O35.06X2	Maternal care for (suspected) central nervous system malformation or damage in fetus, hydrocephaly, fetus 2
O35.06X3	Maternal care for (suspected) central nervous system malformation or damage in fetus, hydrocephaly, fetus 3
O35.06X4	Maternal care for (suspected) central nervous system malformation or damage in fetus, hydrocephaly, fetus 4
O35.06X5	Maternal care for (suspected) central nervous system malformation or damage in fetus, hydrocephaly, fetus 5
O35.06X9	Maternal care for (suspected) central nervous system malformation or damage in fetus, hydrocephaly, other fetus
O35.07X0	Maternal care for (suspected) central nervous system malformation or damage in fetus, microcephaly, not applicable or unspecified
O35.07X1	Maternal care for (suspected) central nervous system malformation or damage in fetus, microcephaly, fetus 1
O35.07X2	Maternal care for (suspected) central nervous system malformation or damage in fetus, microcephaly, fetus 2
O35.07X3	Maternal care for (suspected) central nervous system malformation or damage in fetus, microcephaly, fetus 3
O35.07X4	Maternal care for (suspected) central nervous system malformation or damage in fetus, microcephaly, fetus 4
O35.07X5	Maternal care for (suspected) central nervous system malformation or damage in fetus, microcephaly, fetus 5
O35.07X9	Maternal care for (suspected) central nervous system malformation or damage in fetus, microcephaly, other fetus
O35.08X0	Maternal care for (suspected) central nervous system malformation or damage in fetus, spina bifida, not applicable or unspecified
O35.08X1	Maternal care for (suspected) central nervous system malformation or damage in fetus, spina bifida, fetus 1
O35.08X2	Maternal care for (suspected) central nervous system malformation or damage in fetus, spina bifida, fetus 2
O35.08X3	Maternal care for (suspected) central nervous system malformation or damage in fetus, spina bifida, fetus 3
O35.08X4	Maternal care for (suspected) central nervous system malformation or damage in fetus, spina bifida, fetus 4
O35.08X5	Maternal care for (suspected) central nervous system malformation or damage in fetus, spina bifida, fetus 5
O35.08X9	Maternal care for (suspected) central nervous system malformation or damage in fetus, spina bifida, other fetus
O35.09X0	Maternal care for (suspected) other central nervous system malformation or damage in fetus, not applicable or unspecified
O35.09X1	Maternal care for (suspected) other central nervous system malformation or damage in fetus, fetus 1
O35.09X2	Maternal care for (suspected) other central nervous system malformation or damage in fetus, fetus 2
O35.09X3	Maternal care for (suspected) other central nervous system malformation or damage in fetus, fetus 3
O35.09X4	Maternal care for (suspected) other central nervous system malformation or damage in fetus, fetus 4
O35.09X5	Maternal care for (suspected) other central nervous system malformation or damage in fetus, fetus 5

Diagnosis Code	Description
O35.09X9	Maternal care for (suspected) other central nervous system malformation or damage in fetus, other fetus
O35.10X0	Maternal care for (suspected) chromosomal abnormality in fetus, unspecified, not applicable, or unspecified
O35.10X1	Maternal care for (suspected) chromosomal abnormality in fetus, unspecified, fetus 1
O35.10X2	Maternal care for (suspected) chromosomal abnormality in fetus, unspecified, fetus 2
O35.10X3	Maternal care for (suspected) chromosomal abnormality in fetus, unspecified, fetus 3
O35.10X4	Maternal care for (suspected) chromosomal abnormality in fetus, unspecified, fetus 4
O35.10X5	Maternal care for (suspected) chromosomal abnormality in fetus, unspecified, fetus 5
O35.10X9	Maternal care for (suspected) chromosomal abnormality in fetus, unspecified, other fetus
O35.11X0	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 13, not applicable or unspecified
O35.11X1	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 13, fetus 1
O35.11X2	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 13, fetus 2
O35.11X3	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 13, fetus 3
O35.11X4	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 13, fetus 4
O35.11X5	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 13, fetus 5
O35.11X9	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 13, other fetus
O35.12X0	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 18, not applicable or unspecified
O35.12X1	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 18, fetus 1
O35.12X2	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 18, fetus 2
O35.12X3	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 18, fetus 3
O35.12X4	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 18, fetus 4
O35.12X5	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 18, fetus 5
O35.12X9	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 18, other fetus
O35.13X0	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 21, not applicable or unspecified
O35.13X1	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 21, fetus 1
O35.13X2	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 21, fetus 2
O35.13X3	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 21, fetus 3
O35.13X4	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 21, fetus 4
O35.13X5	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 21, fetus 5
O35.13X9	Maternal care for (suspected) chromosomal abnormality in fetus, Trisomy 21, other fetus
O35.14X0	Maternal care for (suspected) chromosomal abnormality in fetus, Turner Syndrome, not applicable or unspecified
O35.14X1	Maternal care for (suspected) chromosomal abnormality in fetus, Turner Syndrome, fetus 1
O35.14X2	Maternal care for (suspected) chromosomal abnormality in fetus, Turner Syndrome, fetus 2
O35.14X3	Maternal care for (suspected) chromosomal abnormality in fetus, Turner Syndrome, fetus 3
O35.14X4	Maternal care for (suspected) chromosomal abnormality in fetus, Turner Syndrome, fetus 4
O35.14X5	Maternal care for (suspected) chromosomal abnormality in fetus, Turner Syndrome, fetus 5
O35.14X9	Maternal care for (suspected) chromosomal abnormality in fetus, Turner Syndrome, other fetus
O35.15X0	Maternal care for (suspected) chromosomal abnormality in fetus, sex chromosome abnormality, not applicable or unspecified
O35.15X1	Maternal care for (suspected) chromosomal abnormality in fetus, sex chromosome abnormality, fetus 1

Diagnosis Code	Description
O35.15X2	Maternal care for (suspected) chromosomal abnormality in fetus, sex chromosome abnormality, fetus 2
O35.15X3	Maternal care for (suspected) chromosomal abnormality in fetus, sex chromosome abnormality, fetus 3
O35.15X4	Maternal care for (suspected) chromosomal abnormality in fetus, sex chromosome abnormality, fetus 4
O35.15X5	Maternal care for (suspected) chromosomal abnormality in fetus, sex chromosome abnormality, fetus 5
O35.15X9	Maternal care for (suspected) chromosomal abnormality in fetus, sex chromosome abnormality, other fetus
O35.19X0	Maternal care for (suspected) chromosomal abnormality in fetus, other chromosomal abnormality, not applicable or unspecified
O35.19X1	Maternal care for (suspected) chromosomal abnormality in fetus, other chromosomal abnormality, fetus 1
O35.19X2	Maternal care for (suspected) chromosomal abnormality in fetus, other chromosomal abnormality, fetus 2
O35.19X3	Maternal care for (suspected) chromosomal abnormality in fetus, other chromosomal abnormality, fetus 3
O35.19X4	Maternal care for (suspected) chromosomal abnormality in fetus, other chromosomal abnormality, fetus 4
O35.19X5	Maternal care for (suspected) chromosomal abnormality in fetus, other chromosomal abnormality, fetus 5
O35.19X9	Maternal care for (suspected) chromosomal abnormality in fetus, other chromosomal abnormality, other fetus
O35.2XX0	Maternal care for (suspected) hereditary disease in fetus, not applicable or unspecified
O35.2XX1	Maternal care for (suspected) hereditary disease in fetus, fetus 1
O35.2XX2	Maternal care for (suspected) hereditary disease in fetus, fetus 2
O35.2XX3	Maternal care for (suspected) hereditary disease in fetus, fetus 3
O35.2XX4	Maternal care for (suspected) hereditary disease in fetus, fetus 4
O35.2XX5	Maternal care for (suspected) hereditary disease in fetus, fetus 5
O35.2XX9	Maternal care for (suspected) hereditary disease in fetus, other fetus
O35.8XX0	Maternal care for other (suspected) fetal abnormality and damage, not applicable or unspecified
O35.8XX1	Maternal care for other (suspected) fetal abnormality and damage, fetus 1
O35.8XX2	Maternal care for other (suspected) fetal abnormality and damage, fetus 2
O35.8XX3	Maternal care for other (suspected) fetal abnormality and damage, fetus 3
O35.8XX4	Maternal care for other (suspected) fetal abnormality and damage, fetus 4
O35.8XX5	Maternal care for other (suspected) fetal abnormality and damage, fetus 5
O35.8XX9	Maternal care for other (suspected) fetal abnormality and damage, other fetus
O35.AXX0	Maternal care for other (suspected) fetal abnormality and damage, fetal facial anomalies, not applicable or unspecified
O35.AXX1	Maternal care for other (suspected) fetal abnormality and damage, fetal facial anomalies, fetus 1
O35.AXX2	Maternal care for other (suspected) fetal abnormality and damage, fetal facial anomalies, fetus 2
O35.AXX3	Maternal care for other (suspected) fetal abnormality and damage, fetal facial anomalies, fetus 3
O35.AXX4	Maternal care for other (suspected) fetal abnormality and damage, fetal facial anomalies, fetus 4
O35.AXX5	Maternal care for other (suspected) fetal abnormality and damage, fetal facial anomalies, fetus 5
O35.AXX9	Maternal care for other (suspected) fetal abnormality and damage, fetal facial anomalies, other fetus
O35.BXX0	Maternal care for other (suspected) fetal abnormality and damage, fetal cardiac anomalies, not applicable or unspecified

Diagnosis Code	Description
O35.BXX1	Maternal care for other (suspected) fetal abnormality and damage, fetal cardiac anomalies, fetus 1
O35.BXX2	Maternal care for other (suspected) fetal abnormality and damage, fetal cardiac anomalies, fetus 2
O35.BXX3	Maternal care for other (suspected) fetal abnormality and damage, fetal cardiac anomalies, fetus 3
O35.BXX4	Maternal care for other (suspected) fetal abnormality and damage, fetal cardiac anomalies, fetus 4
O35.BXX5	Maternal care for other (suspected) fetal abnormality and damage, fetal cardiac anomalies, fetus 5
O35.BXX9	Maternal care for other (suspected) fetal abnormality and damage, fetal cardiac anomalies, other fetus
O35.CXX0	Maternal care for other (suspected) fetal abnormality and damage, fetal pulmonary anomalies, not applicable or unspecified
O35.CXX1	Maternal care for other (suspected) fetal abnormality and damage, fetal pulmonary anomalies, fetus 1
O35.CXX2	Maternal care for other (suspected) fetal abnormality and damage, fetal pulmonary anomalies, fetus 2
O35.CXX3	Maternal care for other (suspected) fetal abnormality and damage, fetal pulmonary anomalies, fetus 3
O35.CXX4	Maternal care for other (suspected) fetal abnormality and damage, fetal pulmonary anomalies, fetus 4
O35.CXX5	Maternal care for other (suspected) fetal abnormality and damage, fetal pulmonary anomalies, fetus 5
O35.CXX9	Maternal care for other (suspected) fetal abnormality and damage, fetal pulmonary anomalies, other fetus
O35.DXX0	Maternal care for other (suspected) fetal abnormality and damage, fetal gastrointestinal anomalies, not applicable or unspecified
O35.DXX1	Maternal care for other (suspected) fetal abnormality and damage, fetal gastrointestinal anomalies, fetus 1
O35.DXX2	Maternal care for other (suspected) fetal abnormality and damage, fetal gastrointestinal anomalies, fetus 2
O35.DXX3	Maternal care for other (suspected) fetal abnormality and damage, fetal gastrointestinal anomalies, fetus 3
O35.DXX4	Maternal care for other (suspected) fetal abnormality and damage, fetal gastrointestinal anomalies, fetus 4
O35.DXX5	Maternal care for other (suspected) fetal abnormality and damage, fetal gastrointestinal anomalies, fetus 5
O35.DXX9	Maternal care for other (suspected) fetal abnormality and damage, fetal gastrointestinal anomalies, other fetus
O35.EXX0	Maternal care for other (suspected) fetal abnormality and damage, fetal genitourinary anomalies, not applicable or unspecified
O35.EXX1	Maternal care for other (suspected) fetal abnormality and damage, fetal genitourinary anomalies, fetus 1
O35.EXX2	Maternal care for other (suspected) fetal abnormality and damage, fetal genitourinary anomalies, fetus 2
O35.EXX3	Maternal care for other (suspected) fetal abnormality and damage, fetal genitourinary anomalies, fetus 3
O35.EXX4	Maternal care for other (suspected) fetal abnormality and damage, fetal genitourinary anomalies, fetus 4
O35.EXX5	Maternal care for other (suspected) fetal abnormality and damage, fetal genitourinary anomalies, fetus 5
O35.EXX9	Maternal care for other (suspected) fetal abnormality and damage, fetal genitourinary anomalies, other fetus

Diagnosis Code	Description
O35.FXX0	Maternal care for other (suspected) fetal abnormality and damage, fetal musculoskeletal anomalies of trunk, not applicable or unspecified
O35.FXX1	Maternal care for other (suspected) fetal abnormality and damage, fetal musculoskeletal anomalies of trunk, fetus 1
O35.FXX2	Maternal care for other (suspected) fetal abnormality and damage, fetal musculoskeletal anomalies of trunk, fetus 2
O35.FXX3	Maternal care for other (suspected) fetal abnormality and damage, fetal musculoskeletal anomalies of trunk, fetus 3
O35.FXX4	Maternal care for other (suspected) fetal abnormality and damage, fetal musculoskeletal anomalies of trunk, fetus 4
O35.FXX5	Maternal care for other (suspected) fetal abnormality and damage, fetal musculoskeletal anomalies of trunk, fetus 5
O35.FXX9	Maternal care for other (suspected) fetal abnormality and damage, fetal musculoskeletal anomalies of trunk, other fetus
O35.GXX0	Maternal care for other (suspected) fetal abnormality and damage, fetal upper extremities anomalies, not applicable or unspecified
O35.GXX1	Maternal care for other (suspected) fetal abnormality and damage, fetal upper extremities anomalies, fetus 1
O35.GXX2	Maternal care for other (suspected) fetal abnormality and damage, fetal upper extremities anomalies, fetus 2
O35.GXX3	Maternal care for other (suspected) fetal abnormality and damage, fetal upper extremities anomalies, fetus 3
O35.GXX4	Maternal care for other (suspected) fetal abnormality and damage, fetal upper extremities anomalies, fetus 4
O35.GXX5	Maternal care for other (suspected) fetal abnormality and damage, fetal upper extremities anomalies, fetus 5
O35.GXX9	Maternal care for other (suspected) fetal abnormality and damage, fetal upper extremities anomalies, other fetus
O35.HXX0	Maternal care for other (suspected) fetal abnormality and damage, fetal lower extremities anomalies, not applicable or unspecified
O35.HXX1	Maternal care for other (suspected) fetal abnormality and damage, fetal lower extremities anomalies, fetus 1
O35.HXX2	Maternal care for other (suspected) fetal abnormality and damage, fetal lower extremities anomalies, fetus 2
O35.HXX3	Maternal care for other (suspected) fetal abnormality and damage, fetal lower extremities anomalies, fetus 3
O35.HXX4	Maternal care for other (suspected) fetal abnormality and damage, fetal lower extremities anomalies, fetus 4
O35.HXX5	Maternal care for other (suspected) fetal abnormality and damage, fetal lower extremities anomalies, fetus 5
O35.HXX9	Maternal care for other (suspected) fetal abnormality and damage, fetal lower extremities anomalies, other fetus
O36.4XX0	Maternal care for intrauterine death, not applicable or unspecified
O36.4XX1	Maternal care for intrauterine death, fetus 1
O36.4XX2	Maternal care for intrauterine death, fetus 2
O36.4XX3	Maternal care for intrauterine death, fetus 3
O36.4XX4	Maternal care for intrauterine death, fetus 4
O36.4XX5	Maternal care for intrauterine death, fetus 5
O36.4XX9	Maternal care for intrauterine death, other fetus
P95	Stillbirth

Diagnosis Code	Description
QA0.0159	Neurodevelopmental disorder, related to other genes associated with transcription and gene expression
QA0.8	Other neurodevelopmental disorders related to pathogenic variants in other specific genes
Q20.1	Double outlet right ventricle
Q20.2	Double outlet left ventricle
Q20.3	Discordant ventriculoarterial connection
Q20.4	Double inlet ventricle
Q20.5	Discordant atrioventricular connection
Q20.6	Isomerism of atrial appendages
Q20.8	Other congenital malformations of cardiac chambers and connections
Q20.9	Congenital malformation of cardiac chambers and connections, unspecified
Q21.0	Ventricular septal defect
Q21.10	Atrial septal defect, unspecified
Q21.11	Secundum atrial septal defect
Q21.12	Patent foramen ovale
Q21.13	Coronary sinus atrial septal defect
Q21.14	Superior sinus venosus atrial septal defect
Q21.15	Inferior sinus venosus atrial septal defect
Q21.16	Sinus venosus atrial septal defect, unspecified
Q21.19	Other specified atrial septal defect
Q21.20	Atrioventricular septal defect, unspecified as to partial or complete
Q21.21	Partial atrioventricular septal defect
Q21.22	Transitional atrioventricular septal defect
Q21.23	Complete atrioventricular septal defect
Q21.3	Tetralogy of Fallot
Q21.4	Aortopulmonary septal defect
Q21.8	Other congenital malformations of cardiac septa
Q21.9	Congenital malformation of cardiac septum, unspecified
Q22.0	Pulmonary valve atresia
Q22.1	Congenital pulmonary valve stenosis
Q22.2	Congenital pulmonary valve insufficiency
Q22.3	Other congenital malformations of pulmonary valve
Q22.4	Congenital tricuspid stenosis
Q22.5	Ebstein's anomaly
Q22.6	Hypoplastic right heart syndrome
Q22.8	Other congenital malformations of tricuspid valve
Q22.9	Congenital malformation of tricuspid valve, unspecified
Q23.0	Congenital stenosis of aortic valve
Q23.1	Congenital insufficiency of aortic valve
Q23.2	Congenital mitral stenosis
Q23.3	Congenital mitral insufficiency
Q23.4	Hypoplastic left heart syndrome
Q23.81	Bicuspid aortic valve
Q23.82	Congenital mitral valve cleft leaflet
Q23.88	Other congenital malformations of aortic and mitral valves

Diagnosis Code	Description
Q23.9	Congenital malformation of aortic and mitral valves, unspecified
Q24.0	Dextrocardia
Q24.1	Levocardia
Q24.2	Cor triatriatum
Q24.3	Pulmonary infundibular stenosis
Q24.4	Congenital subaortic stenosis
Q24.5	Malformation of coronary vessels
Q24.6	Congenital heart block
Q24.8	Other specified congenital malformations of heart
Q24.9	Congenital malformation of heart, unspecified
Q87.86	Kleefstra syndrome
Q89.7	Multiple congenital malformations, not elsewhere classified
Q89.89	Other specified congenital malformations
Q89.9	Congenital malformation, unspecified
Q90.0	Trisomy 21, nonmosaicism (meiotic nondisjunction)
Q90.1	Trisomy 21, mosaicism (mitotic nondisjunction)
Q90.2	Trisomy 21, translocation
Q90.9	Down syndrome, unspecified
Q91.0	Trisomy 18, nonmosaicism (meiotic nondisjunction)
Q91.1	Trisomy 18, mosaicism (mitotic nondisjunction)
Q91.2	Trisomy 18, translocation
Q91.3	Trisomy 18, unspecified
Q91.4	Trisomy 13, nonmosaicism (meiotic nondisjunction)
Q91.5	Trisomy 13, mosaicism (mitotic nondisjunction)
Q91.6	Trisomy 13, translocation
Q91.7	Trisomy 13, unspecified
Q92.0	Whole chromosome trisomy, nonmosaicism (meiotic nondisjunction)
Q92.1	Whole chromosome trisomy, mosaicism (mitotic nondisjunction)
Q92.2	Partial trisomy
Q92.5	Duplications with other complex rearrangements
Q92.61	Marker chromosomes in normal individual
Q92.62	Marker chromosomes in abnormal individual
Q92.7	Triploidy and polyploidy
Q92.8	Other specified trisomies and partial trisomies of autosomes
Q92.9	Trisomy and partial trisomy of autosomes, unspecified
Q93.0	Whole chromosome monosomy, nonmosaicism (meiotic nondisjunction)
Q93.1	Whole chromosome monosomy, mosaicism (mitotic nondisjunction)
Q93.2	Chromosome replaced with ring, dicentric or isochromosome
Q93.3	Deletion of short arm of chromosome 4
Q93.4	Deletion of short arm of chromosome 5
Q93.7	Deletions with other complex rearrangements
Q93.51	Angelman syndrome
Q93.52	Phelan-McDermid syndrome
Q93.59	Other deletions of part of a chromosome
Q93.81	Velo-cardio-facial syndrome

Diagnosis Code	Description
Q93.82	Williams syndrome
Q93.88	Other microdeletions
Q93.89	Other deletions from the autosomes
Q93.9	Deletion from autosomes, unspecified
Q95.2	Balanced autosomal rearrangement in abnormal individual
Q95.3	Balanced sex/autosomal rearrangement in abnormal individual
Q99.89	Other specified chromosome abnormalities
Q99.9	Chromosomal abnormality, unspecified
R48.0	Dyslexia and alexia
R62.59	Other lack of expected normal physiological development in childhood
R89.8	Other abnormal findings in specimens from other organs, systems, and tissues
Z14.1	Cystic fibrosis carrier
Z14.8	Genetic carrier of other disease
Z36.0	Encounter for antenatal screening for chromosomal anomalies
Z37.1	Single stillbirth
Z37.3	Twins, one liveborn and one stillborn
Z37.4	Twins, both stillborn
Z37.60	Multiple births, unspecified, some liveborn
Z37.61	Triplets, some liveborn
Z37.62	Quadruplets, some liveborn
Z37.63	Quintuplets, some liveborn
Z37.64	Sextuplets, some liveborn
Z37.69	Other multiple births, some liveborn
Z37.7	Other multiple births, all stillborn
Z87.74	Personal history of (corrected) congenital malformations of heart and circulatory system

Description of Services

Genetic counseling is strongly recommended prior to chromosome microarray testing [also called chromosome microarray analysis (CMA)] in order to inform persons being tested about the advantages and limitations of the test as applied to their unique situation. CMA includes array comparative genomic hybridization (aCGH) and/or single-nucleotide polymorphism (SNP) array (Levy and Wapner, 2018).

Chromosome abnormalities are a well-established cause of congenital anomalies, dysmorphic features, Developmental Delay (DD), Intellectual Disability (ID), and other neurodevelopmental disorders. There are two types of CMA that are used for the detection of chromosomal abnormalities: aCGH and SNP array. These tests analyze multiple sequences of deoxyribonucleic acid (DNA) by identifying deletions and duplications across the genome simultaneously. The chromosomal microarray may be targeted in nature, assaying certain regions of the genome known to be associated with a specific syndrome or phenotype and/or may be genome-wide (Shaffer et al., 2007). Currently, most clinical applications of CMA are being investigated for the diagnosis of chromosomal abnormalities in fetuses and newborns, and in children with developmental disorders. For diagnostic prenatal testing, CMA requires an invasive procedure (e.g., amniocentesis or chorionic villous sampling) to collect fetal cells.

SNP array testing and aCGH are used for the detection of genomic copy number variations (CNVs). CNVs are alterations that include deletion and/or duplication of one or more sections of DNA. This method allows the detection of chromosome imbalances that can provide more information than is detected by conventional chromosome analysis [e.g., standard karyotype or fluorescence in situ hybridization (FISH)]. The aCGH approach detects CNVs of a DNA sequence in an individual by comparing it to a control. The SNP array approach detects CNVs by using DNA probes that are specific to a single base pair site in the genome. The copy number is quantified by either hybridization of the individual's DNA and control DNA (aCGH) or comparison of the individual's DNA to a control reference DNA sequence (SNP array). Areas of unequal hybridization (aCGH) or differences between an individual and reference DNA (SNP array) signify a DNA alteration, such as large deletions or duplications. CNVs may be benign, with no effect on clinical phenotype, or may be pathogenic and result in a variety of phenotypic abnormalities (Kearney et al., 2011). If a CNV of unknown clinical significance is detected, a genomic database is used to determine if the abnormality has been previously reported and if it has been associated with a benign or proposed pathogenic condition. The disadvantages of CMA include the detection of variants of unknown clinical significance, false positive results that will require further testing, and the inability to detect certain chromosomal abnormalities such as balanced rearrangements where there is no net gain or loss of the chromosomal material (Fruhman and Van den Veyver, 2010; Bui et al., 2011).

Clinical Evidence

Use in Obstetrics

A single-center, prospective cohort study was conducted by Li et al. (2025) to explore the impact of the use of chromosome microarray analysis (CMA) to evaluate confirmed cases of fetal growth restriction (FGR). A total of 182 individuals with singleton pregnancies and a diagnosis of FGR were enrolled from a medical center in China. The cohort was divided into three categories: isolated FGR, FGR with ultrasound soft marker anomalies, and FGR with structural malformations. Amniocentesis was performed on all participants and both chromosome karyotyping and CMA were completed for each individual. In the group of participants with FGR and structural malformations, the researchers found the detection rates of pathogenic copy number variations (pCNVs) to be significantly higher than those found in the group with FGR and abnormal ultrasound soft markers and those with isolated FGR. (19% vs 1.5% and 2.1%, respectively, $X^2 = 9.33$, $p = 0.005$). Fetuses with multiple system malformations had a significantly higher diagnostic rate of chromosomal variations than fetuses with single system malformations (60% vs 6.3%; $p = 0.028$). Notably, factors such as advanced maternal age, early-onset FGR, and severity of FGR were not found to impact the diagnostic rates of chromosomal variations in this study. Based on these results, the authors propose that the chromosomal variations associated with FGR plus structural anomalies detected via ultrasound may pose significant risk, especially as the number of organ systems involved increases. They recommend standard genetic assessments in cases of FGR occurring after 32 weeks gestation as well as before and propose that submicroscopic imbalances at Xp22.33 and Xq28 may be related to the pathogenesis of FGR. This, however, will require further investigation. The study was limited by its small sample size from only one facility; the authors encourage additional study of the value of CMA in cases of FGR with ultrasound soft marker abnormalities and continue to advocate for the use of CMA as a primary tool for prenatal diagnostics in older pregnant individuals and those with severe FGR despite the findings of this study.

Nguyen et al. (2025) used single-nucleotide polymorphism (SNP)-based CMA to help identify the genetic variations present in fetuses found to have intrauterine growth restriction (IUGR) with malformations identified on ultrasound. This cross-sectional study enrolled 129 individuals aged 18 to 48 whose fetuses were diagnosed with IUGR. Of the 129 cases of IUGR, one malformation only was detected in 83% of the cases, 16% had two malformations, and 1% had three or more malformations. The majority of malformations were related to the cardiovascular system. Of the 75 cases where amniocentesis with karyotyping and SNP array testing were performed, 26 (35%) had genetic abnormalities identified. When comparing the findings of SNP array testing and karyotyping, SNP testing detected more than twice the number of total cases, identifying genetic anomalies that may have otherwise been missed by karyotyping. Although limited by its small size and observational design, this study's outcomes led the authors to infer that CMA technology is more effective in pinpointing genetic causes of IUGR and to recommend that CMA using array SNP should be used in cases of IUGR and congenital malformations.

In a Chinese single-center study, Lu et al. (2024) assessed the clinical utility of CMA performed in cases of pregnancies where the fetus was found to have congenital heart defects (CHD) identified through standard ultrasound anatomy scans, then confirmed via echocardiography. The prevalence of chromosomal abnormalities in these cases was also ascertained; both standard karyotyping and CMA were performed on all cases. A total of 642 cases of fetal CHD were evaluated over a six-year timespan. The researchers determined that, in this study, the diagnostic yield of CMA for fetuses with CHD was 15.3% (98/642), which was substantially higher than the diagnostic yield of standard karyotyping at 8.3% (53/642). Overall, the detection rate of clinically meaningful chromosome anomalies was significantly increased in the group with CHD plus extracardiac structural anomalies when compared with the isolated CHD group (33.1% vs 9.9%, $p < 0.0001$.) Based on their findings, the authors recommend CMA as a first-tier test for fetuses found to have CHD, with special consideration given to cases of CHD with additional structural abnormalities or soft markers. The study was limited by the need for individuals to pay for invasive prenatal testing and the refusal of some participants to engage in further testing, leading to selection bias. In addition, the majority of participants declined follow-up whole exome sequencing (WES), which could have led to more complete genetic diagnoses.

Another study assessing the use of SNP-based CMA to identify underlying genetic causes for fetal cardiac ultrasound abnormalities was undertaken by Ye et al. (2024). This study included 2092 pregnant individuals who were divided into groups based on presence or absence of structural abnormalities identified via ultrasound as well as the specific type of abnormality found. Each participant received prenatal invasive diagnostic testing. Similar to Lu et al., above, the authors found that fetuses with non-isolated CHD had the highest frequency of overall chromosome abnormalities when compared to the isolated CHD group, the non-CHD group, and the control group (42.6% vs 14.1%, 14.9%, and 9.4% respectively). They suggest that SNP-array based CMA is highly effective in boosting the diagnosis of abnormal copy number variations (CNVs) in fetuses with CHD but also emphasize the complexity of the etiologies of CHD, recommending further research that investigates the underlying mechanisms leading to CHD.

To examine diagnostic yields of genomic disorders and syndromic pCNVs associated with pregnancy loss and to approximate the risk of spontaneous abortion (SAB) by comparing the incidence of genomic disorders and syndromic pCNVs between products of conception (POC) and infants, Peng et al. (2023) performed a systematic review and meta-analysis of seven case series where CMA was used to test POC. Based on the meta-analysis of 35,130 results of cytogenomic tests on POC, the estimated diagnostic yields for chromosomal abnormalities and pCNVs were 49.9% (n = 17,548) and 2.5% (n = 957), respectively. After further refinement of pCNV categories, diagnostic yield was found to be 0.8% (n = 296) for genomic disorders and syndromic pCNVs, accounting for approximately 31% of the pCNVs detected overall. Two of the studies were noted to have lower yields of chromosome abnormalities and a higher yield of pCNVs; the authors speculate that this may have been due to the classification of larger terminal and interstitial imbalances, derivative chromosomes, and complex rearrangements into pCNVs. The overall incidence of genomic disorders and syndromic pCNVs in POC was collectively calculated to be 1/150. Newborn incidence was estimated from population genetic studies and a case series of 32,587 children with DD where pCNVs were identified in 2312 individuals (Girirajan et al., 2012). When compared, newborn occurrence of ten genomic disorders and two syndromic pCNVs were significantly lower than that found in POC ($p < 0.05$). An additional five genomic disorders and two syndromic pCNVs were also found to have lower incidence in newborns than in POC, but the differences were statistically insignificant. Altogether, newborn incidence of genomic disorders and syndromic pCNVs was 1/540; substantially less than the corresponding findings of 1/150 in POC ($p < 0.05$). The authors calculated the overall risk of SAB for major genomic disorders and syndromic pCNVs to be 38%; this is significantly lower than the overall risk of SAB for chromosomal abnormalities (94%). They suggest that their results may assist with evidence-based interpretation of genomic disorders and syndromic pCNVs detected via CMA in prenatal diagnosis and provide better understanding of the relationship between genomic disorders and pCNVs and pregnancy loss. Noted limitations include study heterogeneity and gender bias for certain disorders, as well as the potential for impact to newborn incidence from certain genomic anomalies in specific ethnic groups. Additional large, population genetic studies across varying ethnic groups to better refine the evaluation of genomic disorders and syndromic pCNVs in newborns is recommended.

To more accurately assess the risk of chromosome anomalies in fetuses diagnosed with CHD, Wang et al. (2023) performed a meta-analysis of 4 prospective and 41 retrospectives studies including 16,484 fetuses with CHD. A secondary objective was the quantification of the prevalence of various chromosome abnormalities in fetuses with CHD. Results of the meta-analysis revealed a pooled proportion of 23% for overall chromosome abnormalities, 19% for aneuploidies, 2% for 22q11 deletion, and 4% for other CNVs. Of note, the rate of 2% for 22q11 microdeletions was significantly lower than the 4.2-9.6% rate found in other published studies (Hou et al., 2020, Hureaux et al., 2019, Maran et al., 2020). However, many of the incorporated studies did not include comprehensive outcomes and differing detection methods were used across studies, a limitation which may have led to an underestimation of the rate of 22q11 deletion. Pooled proportion of overall chromosome abnormalities in isolated CHD was 16% [95% confidence interval (CI) 13%-20%] and in non-isolated CHD was 37% (95% CI 29%-44%), suggesting that fetuses with CHD along with other structural anomalies are at a higher risk of chromosome abnormalities. In addition, incidence of chromosome abnormalities was higher in septal defects than in conotruncal or other defects [odds ratio (OR) 1.60 and 3.61, respectively]. The authors indicate that their findings add to the evidence demonstrating relationships between CHD subtypes and chromosome abnormalities which will lead to improvements in genetic counseling and clinical decision-making. They recommend CMA for CHD if karyotyping for FISH is normal, especially in cases of non-isolated CHD and septal defects, where the incidence of chromosome abnormalities is higher. The heterogeneity of included studies was high, however, and interpretation processes were not described in most included studies, which limits the application of this meta-analysis. In addition, all but four of the studies were retrospective in design. Further large, high-quality, prospective studies focused on the specific pathogenicity of CNVs and variants of uncertain significance (VUS) in fetuses with diagnoses of CHD are recommended. Publication by Sagi-Dain et al. (2018), previously discussed in evidence, was included in this meta-analysis.

In a systematic review, meta-analysis, and case series, Mastromoro et al. (2022a) studied diagnostic yields of genetic testing in cases where increased nuchal translucency (NT) was identified and compared these with results found in fetuses where cystic hygroma was detected, aiming to identify the differing chromosomal, genomic, and monogenic conditions present in this phenotypic spectrum. In addition, a case series including dicentric fetal findings where karyotyping, CMA, and RASopathy panel was performed was gathered. A cohort of 96 fetuses was evaluated. Fetuses with isolated NT of at least 2.5 mm were found to have karyotype anomalies in 22.76% of cases and an incremental detection rate of 2.35% was identified when CMA was used. Those fetuses having isolated NT ≥ 3 mm resulted in an aneuploidy in 14.36% of cases and an incremental detection rate of 3.89% with CMA. When isolated NT was ≥ 3.5 mm, diagnostic yield of the karyotype was 34.35% with an incremental detection rate for CMA of 4.1%. In this group, the RASopathy panel yielded an incremental diagnostic rate of 1.44% and exome sequencing yielded a 2.44% incremental detection rate. The most frequent finding across the group was karyotype abnormalities regardless of size of NT. Notably, CMA resulted in a substantial diagnostic yield in fetuses where NT was found to be at least 3.5mm. The researchers recommend ongoing research to determine the diagnostic rate of CMA at all levels of increased NT with focus on analysis of monogenic conditions where NT measures between 2.5 and 2.9 mm or 2.5 and 3.4 mm in addition to studies which help define the best diagnostic algorithm which may include exome sequencing. Publication by Egloff et al. (2018), previously discussed in this policy, was included in the systematic review and meta-analysis described above.

Mastromoro et al. (2022b) also performed a systematic review and meta-analysis focused on the incremental diagnostic yield of CMA in isolated cardiovascular abnormalities in fetuses and calculation of specific yield based on each category of heart disease. The end goal was to provide insight for genetic counseling for each subgroup of cardiovascular anomaly. Additionally, a comparison to the existing literature was performed with a group of fetuses (n = 59) who were found to have isolated cardiovascular malformations but a normal karyotype. After application of exclusion criteria, 18 articles were included in the analysis. The researchers found that in pooled cardiovascular anomalies, the diagnostic incremental yield of CMA was 5.79%; this is higher than the average for structural abnormalities, which verifies the importance of this type of testing. In conotruncal malformations, detection rate was highest at 15.93% and yields for ventricular septal defects and aberrant right subclavian artery were lowest at 2.64% and 0.66%, respectively. The majority of heart conditions evaluated yielded a detection rate in the rage of 4.42% to 6.67%, which did not vary greatly from the overall rate for cardiopathic disease. The highest detection rate (11.28%) was found in tetralogy of Fallot (TOF) which is likely due to the relationship with 22q11.2 deletion syndrome. In the group with cardiac anomalies and normal karyotypes, the diagnostic yield was consistent with the existing literature. The authors assert that CMA used to assess the cause of fetal cardiovascular anomalies in the prenatal setting is a helpful tool; information regarding unique risks associated with each type of cardiac malformation is highly valuable when customizing genetic counseling. Publications by Hureaux et al. (2019), Fu et al. (2017), and Shaffer et al. (2012), previously discussed in this policy, were included in this systematic review.

In addition to the studies above, Mastromoro et al. (2022c) performed another systematic review of the literature and meta-analysis, this time focused on examining the diagnostic yield and rates of VUS in a group of fetuses who had undergone non-targeted molecular diagnostic testing including CMA, WES, or whole genome sequencing (WGS) related to findings on ultrasound evaluation. The researchers aimed to provide additional insights into the primary molecular testing modalities used in prenatal diagnostics and their use as part of a multidisciplinary evaluation. For CMA, the overall diagnostic yield for mixed anomalies was 5.72%. This included 2.15% for single soft markers (such as transient minor ultrasound findings), 3.44% for multiple soft markers, 3.66% for single structural anomalies, and 8.57% for multiple structural anomalies. WES demonstrated a high incremental yield with diagnostic rate of 19.47%, including 27.47% for multiple structural abnormalities. Variability was seen related to the characteristics of participants, class of malformations and number of samples available. VUS found for fetuses with structural abnormalities were 2.86% for CMA and 8.32% for WES. Existing data was not able to be used for meta-analysis in WGS. The authors suggest that for structural anomalies in fetuses, CMA is considered a first-tier test and should be used in conjunction with parental segregation and karyotyping. They recommend considering findings of increased NT, short femur, and mild ventriculomegaly to be similar to malformations, separate from other soft markers, and an indication for performing assessment with CMA. They further note that WES presents a very high incremental yield and a substantial VUS rate; as such, the use of WES is recommended for selected cases. Further research focused on which findings should truly be considered “soft” markers is recommended in order to further refine testing recommendations. Publications by Song et al. (2020), Xia et al. (2020), Hureaux et. al. (2019), Egloff et al. (2018), Sagi-Dain et al. (2018), Wang et al. (2018), Peng et al. (2017), Papoulidis et al. (2015), and Shaffer et al. (2012), previously discussed in this policy, were included in this systematic review.

In an attempt to identify possible miscarriage-associated submicroscopic CNVs, target regions of large CNVs, and recognize miscarriage candidate genes, Wang et al. (2020) analyzed 5180 POC samples by quantitative fluorescent-polymerase chain reaction (QF-PCR)/CNV-sequencing and CMA. Significant submicroscopic CNVs were determined by comparing the frequency of recurrent submicroscopic CNVs between cases and a published control cohort. Genes found within critical regions of miscarriage-associated CNVs were prioritized by integrating Residual Variance Intolerance Score and the human gene expression data for identification of possible miscarriage candidate genes. A total of 2955/5033 (59.1%) showed clinically significant chromosomal abnormalities. Three areas of recurring CNVs (microdeletions of 22q11.21, 2q37.3, and 9p24.3p24.2) were detected and considered to be associated with miscarriage. Forty-four critical regions of large CNV were noted which included 14 deletions and 30 duplications. A total of 209 genes were identified as possible miscarriage candidate genes.

Geffen et al. (2020) examined the prevalence of pathogenic and likely-pathogenic variants detected by CMA in pregnancies with ultrasound findings of fetal short long bones. The cohort included 66 cases of CMA performed nationwide with the indication of short long bones; 6% (n = 4) cases had pathogenic/likely pathogenic results. Chromosome anomaly rates were significantly increased compared to the background risk for CNV in pregnancies with no ultrasound abnormalities ($p < 0.001$). The authors reported that the yield of CMA in their study was significantly higher for both isolated and non-isolated cases, for cases in which the lowest determined bone length percentile was over the 3rd percentile (below 5th percentile), and for cases diagnosed with short bones after 22 weeks but not after 24 weeks. They concluded that CMA should be offered in pregnancies with a diagnosis of fetal short long bone due to the significantly higher likelihood of CMA yield compared to background risk in pregnancies with no ultrasound findings.

The University of California-San Francisco performed a retrospective study of prenatally diagnosed non-immune hydrops fetalis (NIHF) from 2008-2018. Mardy et al. (2020) reported on 131 cases which revealed 43/44 cases had CMA performed and results were categorized as normal or likely benign. One case had a large, pathogenic duplication. The authors stated that these results demonstrated the low diagnostic utility of CMA for NIHF.

Pasternak et al. (2020) analyzed the diagnostic yield of CMA among pregnancies terminated for fetal malformations detected on ultrasound. CMA was performed for 71 pregnancies using fetal or placental deoxyribonucleic acid (DNA). The authors reported that "findings were abnormal in 17 cases (23.9%), 13 of which were detectable by karyotype. The incremental yield of CMA was 4/71 (5.6%); 1/32 (3.1%) for cases with an isolated anomaly and 3/39 (7.7%) for cases with non-isolated anomalies."

A systematic review and meta-analysis was performed by Srebniak et al. (2017). In the initial analysis, 10,614 fetal CMA results were reviewed from ten large studies; 1/119 (0.84%) of cases referred for advanced maternal age (AMA) and/or anxiety revealed a clinically significant CNV (95% CI). An analysis of a subset including eight of the initial 10 studies (10,314 fetuses) demonstrated CNVs associated with early onset syndromes in 1/270 (0.37%) pregnancies (95% CI). A total of 1/909 (0.11%) revealed late-onset diseases, and CNV susceptibility was found in 1/333 (0.3%). By combining the individual risk for CNVs with individual risk for chromosome abnormalities detectable by karyotype, the authors reported an overall risk of greater than 1/180 for a significant cytogenetic abnormality. Because women less than 36 years of age have a higher risk for CNV than for Down syndrome, the authors surmised that all women should be advised of these overall individual risks and not just of individual trisomic risks. Studies by Papoulidis et al. (2015) and Shaffer et al. (2012), previously discussed in this policy, were included in the 2017 Srebniak publication.

In a large cohort study, Maya et al. (2018) evaluated the frequency of penetrance of CNVs in low and high risk prenatal and postnatal samples. The cohort was grouped according to CMA indication with group I including low-risk, prenatal women as the control group; group II including high risk prenatal women with fetuses that had congenital malformations; and group III including post-natal individuals with a variety of genetic based conditions. Within this cohort, 21,594 CMAs were performed and the frequency of high penetrance CNVs was 0.1% in group I, 0.9% in group II, and 2.6% in group III. CNV frequency of moderate penetrance was 0.3%, 0.6%, and 1.2%, respectively, and these differences were statistically significant. The frequency of low-penetrance CNVs was not significantly different among groups: 0.6%, 0.9%, and 1.0%, respectively. The study concluded that high penetrance CNVs may be a factor in heritability of various anomalies, however low penetrance CNVs do not seem to contribute.

Pauta et al. (2017) performed a systemic review of the literature and meta-analysis to determine the utility of CMA by either aCGH or SNP-microarray when compared to traditional karyotyping in early pregnancy loss. In twenty-three studies, 5520 pregnancy losses up to 20 weeks gestational age were reviewed. CMA provided informative results on 95% of cases compared to 67% with karyotyping, and CMA provided a 2% greater yield of pCNVs. The authors concluded that CMA resulted in diagnostic information in early pregnancy loss in significantly more cases when compared to conventional chromosome analysis.

Clinical Practice Guidelines

American College of Medical Genetics and Genomics (ACMG)

The 2018 ACMG clinical practice report on genetic testing after CMA for the diagnosis of neurodevelopmental disability and congenital anomalies (Waggoner et al.) states that "chromosomal microarray (CMA) is recommended as the first-tier test in evaluation of individuals with neurodevelopmental disability and congenital anomalies. CMA may not detect balanced cytogenomic abnormalities or uniparental disomy (UPD), and deletion/duplications and regions of homozygosity may require additional testing to clarify the mechanism and inform accurate counseling."

The ACMG (Cherry et al., 2017) published a practice resource guideline for laboratories addressing diagnostic testing following positive noninvasive prenatal screening (NIPS) which made the following recommendations:

- CMA on CVS or amniocentesis may be used for confirmatory diagnosis for abnormal NIPS results or as a reflex to normal karyotype analysis.
- CMA testing should be utilized for follow-up when small copy number changes are reported as positive on NIPS.
- Testing of POC and/or fetus by karyotype or CMA should be considered on a case basis when prenatal diagnosis is not possible.
- For neonates with abnormal physical findings which are not suggestive of the trisomy suggested by original screening, CMA is recommended.
- CMA is recommended when NIPS sex determination is not concordant with physical examination or other clinical evidence reveals possible disorder of sexual differentiation.

American College of Obstetricians and Gynecologists (ACOG)/Society for Maternal Fetal Medicine (SMFM)

In a 2020 (reaffirmed 2021) Obstetric Care Consensus, ACOG and SMFM address microarray analysis as it relates to the management of stillbirth. Microarray analysis is noted to be the preferred method for evaluating stillbirth as it not only detects aneuploidy but correspondingly detects CNVs that are not measurable by karyotype. Microarray analysis is also more likely to offer a genetic diagnosis due to its success with nonviable tissue, making it particularly valuable in analysis of stillbirths with congenital anomalies or when karyotype outcomes cannot be obtained. The consensus document concludes that incorporating microarray analysis into stillbirth work up results in improvements in test success rates and detection of genetic anomalies compared with conventional testing with karyotype.

In a 2016 Committee Opinion on Microarrays and Next-Generation Sequencing Technology (ACOG, 2016a, reaffirmed 2023), ACOG and SMFM make the following recommendations for the use of chromosomal microarray analysis and newer genetic technologies in prenatal diagnosis:

- Most genetic changes identified by CMA that typically are not identified on standard karyotype are not associated with increasing maternal age; therefore, the use of this test can be considered for all women, regardless of age, who undergo prenatal diagnostic testing.
- Prenatal CMA 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 a CMA can be performed.
- CMA of fetal tissue (i.e., amniotic fluid, placenta, or POC) is recommended in the evaluation of intrauterine fetal 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.
- Comprehensive patient pretest and posttest genetic counseling from an obstetrician–gynecologist or other health care provider with genetics expertise regarding the benefits, limitations, and results of chromosomal microarray analysis is essential. CMA should not be ordered without informed consent, which should include discussion of the potential to identify findings of uncertain significance, non-paternity, consanguinity, and adult-onset disease.

In Practice Bulletin number 162 (ACOG, 2016b) which addresses prenatal diagnostic testing for genetic disorders, ACOG and SMFM recommend the following:

- CMA should be made available to any patient choosing to undergo invasive diagnostic testing (based on good/consistent scientific evidence: Level A).
- CMA should be the primary test (replacing conventional karyotype) for patients undergoing prenatal diagnosis for the indication of a fetal structural abnormality detected by ultrasound (based on good/consistent scientific evidence: Level A).
- Chromosomal microarray analysis may be used to confirm an abnormal FISH test (based on limited or inconsistent scientific evidence: Level B).

Society for Maternal-Fetal Medicine (SMFM)

SMFM Consult Series Number 52 (Martins et al., 2020): Diagnosis and management of FGR recommends:

- Pregnant women should be offered fetal diagnostic testing, including CMA, when FGR is detected and a fetal malformation, polyhydramnios, or both are present, regardless of gestational age.
- Pregnant women should be offered prenatal diagnosis testing with CMA when unexplained isolated FGR is diagnosed < 32 weeks of gestation.

In an SMFM Consult Series publication (2016) on the use of CMA for prenatal diagnosis, SMFM makes the following recommendations:

- CMA should 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).
- Providers should discuss the benefits and limitations of CMA and conventional karyotype with patients who are considering amniocentesis and chorionic villus sampling (CVS) and that both options be available to women who choose to undergo diagnostic testing (GRADE 1B).
- The use of CMA is not recommended as a first-line test to evaluate first trimester pregnancy losses due to limited data (GRADE 1C).
- Pre- and post-test counseling should be performed by trained genetic counselors, geneticists, or other providers with expertise in the complexities of interpreting CMA results (Best practice).

Society of Obstetricians and Gynaecologists of Canada (SOGC)

In guideline number 442, the SOGC addressed the use of CMA in their recommendations regarding screening, diagnosis, and management of FGR in singleton pregnancies (Kingdom et al., 2023). The SOGC indicates that genetic consultation and amniocentesis with CMA of fetal DNA and molecular analysis for congenital infections should be offered to pregnant individuals with suspected early-onset FGR, especially if there is evidence of structural abnormalities, polyhydramnios, or multiple soft markers, when there is no indication of a placental basis for FGR. (Strong recommendation, high quality of evidence)

Society of Obstetricians and Gynaecologists of Canada (SOGC)/Canadian College of Medical Geneticists (CCMG)

A Joint Clinical Practice Guideline of the SOGC and CCMG recommended offering CMA in cases of multiple congenital anomalies revealed on ultrasound (II-1A) or fetal MRI. In addition, CMA was also recommended when single congenital defects in conjunction with other findings (e.g., IUGR, oligohydramnios) are detected. Prenatal CMA should be considered for certain malformations that have a high association with abnormal results. CMA is not recommended for pregnancies that are at low risk for a structural anomaly (Audibert et al., 2017).

An SOGC/CCMG Practice Guideline for the use of CMA for prenatal diagnosis and assessment of fetal loss in Canada (Armour et al., 2018) recommends the following:

- CMA may be offered following normal aneuploidy screen results when multiple fetal malformations are detected (II-1A) or NT ≥ 3.5MM (II-2B).
- Genetic counseling should be provided to obtain informed consent; parental decisions for reporting of incidental findings (II-2A); and for post-test results reporting counseling (III-A).
- CMA resolution should be similar to postnatal CMA panels for the detection of small pathogenic variants.
- VUS smaller than 500 Kb deletion or 1 Mb duplication should not be reported in prenatal setting.
- VUS above such cut-offs should only be reported if there is significant evidence that deletion or duplication or the region may be pathogenic (III-B).
- Secondary findings associated with significant childhood onset conditions should be reported; variants associated with adult-onset conditions should only be reported if previously requested by parents or if disclosure could prevent harm to family members (III-A).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Genetic tests are regulated under the Clinical Laboratory Improvement Amendments (CLIA) of 1988. Refer to the following website for more information: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm124105.htm. (Accessed February 20, 2025)

Refer to the following website for a list of nucleic acid-based tests/platforms that have been cleared or approved by the FDA's Center for Devices and Radiological Heath: https://www.fda.gov/medical-devices/in-vitro-diagnostics/nucleic-acid-based-tests. (Accessed February 20, 2025)

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Policy History/Revision Information

Date	Summary of Changes
06/01/2026	**Applicable Codes** • Added ICD-10 diagnosis codes Q89.89, Q99.89, QA0.0159, and QA0.8 • Removed ICD-10 diagnosis codes Q89.8 and Q99.8 **Supporting Information** • Updated *References* section to reflect the most current information • Archived previous policy version CS017ID.C

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state, or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state, or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state, or contractual requirements for benefit plan coverage govern. Before using this policy, check the federal, state, or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

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