Preimplantation Genetic Testing and Related Services

Policy Number: CS160.N
Effective Date: May 1, 2026

➲ Instructions for Use

Table of Contents **Page**

Application 1
Coverage Rationale 1
Medical Records Documentation Used for Reviews 2
Definitions 2
Applicable Codes 2
Description of Services 4
Clinical Evidence 4
U.S. Food and Drug Administration 18
References 18
Policy History/Revision Information 22
Instructions for Use 22

Related Community Plan Policies

- Cell-Free Fetal DNA Testing
- Chromosome Microarray Testing (Non-Oncology Conditions)
- Whole Exome and Whole Genome Sequencing (Non-Oncology Conditions)

Commercial Policy

- Preimplantation Genetic Testing and Related Services

Related Clinical Guideline

- Fertility Solutions Medical Necessity Clinical Guideline: Infertility

Application

This Medical Policy does not apply to the states listed below; refer to the state-specific policy/guideline, if noted:

State	Policy/Guideline
Idaho	Preimplantation Genetic Testing and Related Services (for Idaho Only)
Indiana	None
Kansas	Preimplantation Genetic Testing and Related Services (for Kansas Only)
Kentucky	Preimplantation Genetic Testing and Related Services (for Kentucky Only)
Nebraska	Preimplantation Genetic Testing and Related Services (for Nebraska Only)
New Jersey	Preimplantation Genetic Testing and Related Services (for New Jersey Only)
New Mexico	Preimplantation Genetic Testing and Related Services (for New Mexico Only)
North Carolina	None
Ohio	Preimplantation Genetic Testing and Related Services (for Ohio Only)
Pennsylvania	Preimplantation Genetic Testing and Related Services (for Pennsylvania Only)
Tennessee	Preimplantation Genetic Testing and Related Services (for Tennessee Only)

Coverage Rationale

Preimplantation Genetic Testing (PGT) is proven and medically necessary only for monogenic/single-gene defects (PGT-M) or inherited structural chromosome rearrangements (PGT-SR) using polymerase chain reaction, next-generation sequencing (i.e., for chromosomal rearrangements), or chromosomal microarray for the following:

- The embryo is at an increased risk of a recognized inherited disorder, with both of the following:
  - The increased risk of a recognized inherited disorder is due to one of the following:
    - Each of the intended parents is a carrier of the same autosomal recessive disease
    - At least one parent is a carrier of an autosomal dominant, sex-linked, or mitochondrial condition
    - At least one parent is a carrier of a structural chromosome rearrangement

- The medical condition being prevented must result in Significant Health Problems or Severe Disability and be caused by a single gene (PGT-M) or structural changes of a parent's chromosome (PGT-SR)

PGT is proven and medically necessary for human leukocyte antigen typing on an embryo in order for the future child to provide bone marrow or blood to treat an affected sibling.

PGT is unproven and not medically necessary for all other populations and conditions due to insufficient evidence of efficacy. This includes but is not limited to PGT using chromosomal microarray, polymerase chain reaction, or next-generation sequencing for the following:

- Aneuploidy screening (PGT-A)
- Determining sex when the embryo is not at risk for a sex-linked disorder
- Predicting risk of polygenic disorders (PGT-P) and/or embryo selection based on polygenic scores

Note: PGT must be ordered after genetic counseling.

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 service requested; refer to the guidelines titled Medical Records Documentation Used for Reviews.

Definitions

Preimplantation Genetic Testing (PGT): A test performed to analyze the DNA from oocytes (polar bodies) or embryos (cleavage stage or blastocyst) for human leukocyte antigen typing or for determining genetic abnormalities. These include the following:

- PGT-A: For aneuploidy screening (formerly preimplantation genetic screening)
- PGT-M: For monogenic/single-gene defects (formerly single-gene preimplantation genetic diagnosis)
- PGT-SR: For chromosomal structural rearrangements (formerly chromosomal preimplantation genetic diagnosis)

(Zegers-Hochschild et al., 2017)

Significant Health Problems or Severe Disability: A disability or impairment that is physical or mental and substantially limits one or more major life activities. The impairment is expected to last at least 12 months or result in death (Department of Labor; Office of Disability Employment Policy; Federal Government Definition for Social Security Disability Benefits).

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
0254U	Reproductive medicine (preimplantation genetic assessment), analysis of 24 chromosomes using embryonic DNA genomic sequence analysis for aneuploidy, and a mitochondrial DNA score in euploid embryos, results reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplications, mosaicism, and segmental aneuploidy, per embryo tested
0552U	Reproductive medicine (preimplantation genetic assessment), analysis for known genetic disorders from trophectoderm biopsy, linkage analysis of disease-causing locus, and when possible, targeted mutation analysis for known familial variant, reported as low-risk or high-risk for familial genetic disorder

CPT Code	Description
0553U	Reproductive medicine (preimplantation genetic assessment), analysis of 24 chromosomes using DNA genomic sequence analysis from embryonic trophectoderm for structural rearrangements, aneuploidy, and a mitochondrial DNA score, results reported as normal/balanced (euploidy/balanced), unbalanced structural rearrangement, monosomy, trisomy, segmental aneuploidy, or mosaic, per embryo tested
0554U	Reproductive medicine (preimplantation genetic assessment), analysis of 24 chromosomes using DNA genomic sequence analysis from trophectoderm biopsy for aneuploidy, ploidy, a mitochondrial DNA score, and embryo quality control, results reported as normal (euploidy), monosomy, trisomy, segmental aneuploidy, triploid, haploid, or mosaic, with quality control results reported as contamination detected or inconsistent cohort when applicable, per embryo tested
0555U	Reproductive medicine (preimplantation genetic assessment), analysis of 24 chromosomes using DNA genomic sequence analysis from embryonic trophectoderm for structural rearrangements, aneuploidy, ploidy, a mitochondrial DNA score, and embryo quality control, results reported as normal/balanced (euploidy/balanced), unbalanced structural rearrangement, monosomy, trisomy, segmental aneuploidy, triploid, haploid, or mosaic, with quality control results reported as contamination detected or inconsistent cohort when applicable, per embryo tested
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
89290	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); less than or equal to 5 embryos
89291	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); greater than 5 embryos
Related Services	
58970	Follicle puncture for oocyte retrieval, any method
58974	Embryo transfer, intrauterine
76948	Ultrasonic guidance for aspiration of ova, imaging supervision and interpretation
89250	Culture of oocyte(s)/embryo(s), less than 4 days
89251	Culture of oocyte(s)/embryo(s), less than 4 days; with co-culture of oocyte(s)/embryos
89253	Assisted embryo hatching, microtechniques (any method)
89254	Oocyte identification from follicular fluid
89255	Preparation of embryo for transfer (any method)
89257	Sperm Identification from aspiration (other than seminal fluid)
89258	Cryopreservation; embryo(s)
89260	Sperm isolation: simple prep (e.g., sperm wash and swim-up) for insemination or diagnosis with semen analysis
89261	Sperm isolation: complex prep (e.g., Percoll gradient, albumin gradient) for insemination or diagnosis with semen analysis
89264	Sperm identification from testis tissue, fresh or cryopreserved
89268	Insemination of oocytes
89272	Extended culture of oocyte(s)/embryo(s), 4-7 days
89280	Assisted oocyte fertilization, microtechnique; less than or equal to 10 oocytes
89281	Assisted oocyte fertilization, microtechnique; greater than 10 oocytes

CPT Code	Description
Related Services	
89342	Storage (per year); embryo(s)
89352	Thawing of cryopreserved; embryo(s)

CPT® is a registered trademark of the American Medical Association

HCPCS Code	Description
S4011	In vitro fertilization; including but not limited to identification and incubation of mature oocytes, fertilization with sperm, incubation of embryo(s), and subsequent visualization for determination of development
S4015	Complete in vitro fertilization cycle, not otherwise specified, case rate
S4016	Frozen in vitro fertilization cycle, case rate
S4022	Assisted oocyte fertilization, case rate
S4037	Cryopreserved embryo transfer, case rate

Description of Services

Genetic counseling is strongly recommended prior to Preimplantation Genetic Testing (PGT) in order to inform persons being tested about the advantages and limitations of the test as applied to their unique situation.

PGT is an analysis performed on an embryo, prior to transfer, to screen for aneuploidy (PGT-A), screen for deletions and duplications of genomic material (generally referred to as copy number variations) or structural rearrangements (PGT-SR), and/or analyze single-gene or other inherited disorders (PGT-M) (American College of Obstetricians and Gynecologists, 2020; reaffirmed 2025). Use of this technology has been theorized to increase the success of infertility treatment (Yan et al., 2021), especially in women who have worse outcomes due to advanced maternal age, history of recurrent miscarriage, failed in vitro fertilization, or a balanced chromosome translocation. In addition, PGT has been explored as a way to enable single-embryo transfer rather than using multiple embryos to increase the odds of having a successful pregnancy, without the risk of a multiple gestation (American College of Obstetricians and Gynecologists, 2020; reaffirmed 2025).

PGT for polygenic disorders (PGT-P) has been proposed to screen for many complex diseases such as breast cancer, hypertension, diabetes, and schizophrenia. The primary theoretical benefit is a decrease in the lifetime risk of polygenic disease in individuals born after PGT-P screening. However, most complex diseases are not solely influenced by genetics but also by environmental, lifestyle, and other factors and by random molecular events. PGT-P also has potential harms; individual and societal ethical implications are currently being explored and studied (Capalbo et al., 2024).

Clinical Evidence

Preimplantation Genetic Testing

Mao et al. (2024) published the results of a meta-analysis that evaluated the risk of adverse obstetric and neonatal outcomes after trophectoderm (TE) biopsy for preimplantation genetic testing (PGT) compared with conventional in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) without PGT. The primary outcomes that were measured were preterm birth (PTB) and low birth weight (LBW) in live birth infants. The secondary outcomes included cesarean delivery, preeclampsia, gestational hypertension, hypertensive disorders of pregnancy, placenta previa, placental abruption, premature rupture of membranes, gestational diabetes, postpartum hemorrhage, fetal growth restriction, small for gestational age, macrosomia, birth defect or congenital malformation (CM), and admission to the neonatal intensive care unit. In all, 13 studies [12 retrospective cohort and one randomized controlled trial (RCT)] that evaluated 11,469 live births after PGT with TE biopsy prior to embryo transfer (ET) and 20,438 live births after IVF or ICSI only were included. Although the odds ratio (OR) of preterm delivery was initially higher in the TE-biopsied group (pooled OR, 1.12; 95% CI, 1.03-1.21), this difference did not persist after sensitivity analysis (OR, 0.97; 95% CI, 0.84-1.11); LBW risk did not increase in the biopsied pregnancy group (pooled OR, 1.01; 95% CI, 0.85-1.20). No significant differences were seen in risk of other obstetric or neonatal outcomes between the biopsy and control groups nor were there differences in perinatal outcomes after subgroup analyses that examined ICSI, frozen-thawed transfer, or single-embryo transfer (SET). The authors concluded that based on the results of this meta-analysis, TE biopsy for PGT did not increase the risk of the defined adverse obstetric or neonatal outcomes compared with standard IVF or ICSI without PGT, but larger, well-designed RCTs are recommended. The results of this meta-analysis are limited by the inability to assess the effect of

underlying infertility status in individuals undergoing PGT and IVF/ICSI. In addition, individuals undergoing PGT have a greater number of optimal embryos available for transfer compared with those undergoing IVF or ICSI without PGT, leading to potential bias. Lastly, most included studies were retrospective cohorts that did not allow for adjustment of confounding factors. Further well-designed RCTs that are focused on TE biopsy safety were recommended by the researchers. Publications by Li et al. (2021) and Yan et al. (2021), previously discussed in this policy, were included in the meta-analysis.

Ginström Ernstad et al. (2023) published the results of a Swedish registry-based study that compared perinatal outcomes in and early childhood health of children born specifically after PGT (n = 390) with those in children who were born after IVF/ICSI (n = 61,060), along with a matched group born after spontaneous conception (n = 42,034). Only singleton pregnancies were included in the analysis, which incorporated births occurring between January 1996 and September 2019. The primary outcomes that were assessed were PTB and LBW. Childhood morbidity was a secondary outcome. Data from participants who had undergone PGT and IVF/ICSI were cross-linked to national health registries, including the Medical Birth Register, Patient Register, and Cause of Death Register. The mean follow-up time in children born after PGT was 4.6 years; in children born after IVF/ICSI, it was 9.0 years, and in children born after spontaneous conception, it was 5.1 years. The analysis revealed that PTB took place in 7.7% of infants who were born after PGT and 7.3% of infants who were born after IVF/ICSI. LBW rates were 4.9% for PGT and 5.2% for IVF/ICSI. The researchers found no difference between these two groups regarding birth defects. However, compared with spontaneous conception, infants born after PGT had a higher risk of PTB [adjusted OR (AOR), 1.73; 95% CI, 1.17-2.58]. In addition, the rate of LBW was 4.9% in the PGT group and 3.2% in the spontaneous conception group (AOR, 1.52; 95% CI, 0.93-2.49). Regarding health in early childhood, no significant differences were found between the PGT group and the all-IVF/ICSI or spontaneous conception group for risk of asthma or allergic disorders. Other health issues, including sepsis, hypothyroidism, attention-deficit/hyperactivity disorder, autism spectrum disorders, intellectual disabilities, cerebral palsy, and epilepsy, were very rare in the PGT group, occurring in a maximum of only three children. Rates of placenta previa and cesarean delivery were not significantly different between the PGT and IVF/ICSI group; however, rates of these maternal complications were significantly higher after PGT compared with spontaneous conception (AOR, 6.46, 95% CI, 3.38-12.37 and AOR, 1.52, 95% CI, 1.20-1.92, respectively). The authors contended that their results indicate that alone, the biopsy that was performed for PGT does not negatively impact maternal, perinatal, or early childhood health outcomes; outcomes for PGT and IVF/ICSI were similar. However, they advised that the results should be interpreted with caution, since the sample size of children born after PGT was small, the follow-up time was generally short, and the number of children with established diagnoses was limited. Additional long-term follow-up studies in children born after PGT are recommended.

The Japan Society of Obstetrics and Gynecology (Iwasa et al., 2023) conducted a multicenter clinical trial to evaluate pregnancy outcomes of PGT testing for aneuploidy (PGT-A) and PGT testing for chromosomal structural rearrangement (PGT-SR). The main outcome that was assessed was ongoing pregnancy rate (OPR) at 12 weeks of gestation. The secondary outcomes included the clinical pregnancy rate per ET and miscarriage rate per pregnancy. Participants in the study were those who had experienced recurrent implantation failure (RIF), recurrent pregnancy loss (RPL), or chromosome structural rearrangement. RIF was the most common indication for PGT-A/-SR, accounting for approximately 70% of the cases. A total of 42,529 blastocysts were biopsied for PGT-A/-SR; 25.5% of the embryos were euploid, 11.7% demonstrated mosaicism, and 61.7% were aneuploid (1.1% were undiagnosable). Overall, 6,080 ETs were performed. The OPR per ET was 56.3%, clinical pregnancy rate per ET was 68.8%, and miscarriage rate per pregnancy was 10.4%. In general, rates of clinical pregnancy and miscarriage were consistent across maternal age. In previous studies, it had been reported that (1) the pregnancy rate per ET was 33.9% and the miscarriage rate per pregnancy was 24.9% in individuals undergoing assisted reproductive technology (ART) in Japan in 2020 and that (2) these rates worsened as individuals aged. Although the study was limited by the lack of controls and because combined data were used for RIF, RPL, and chromosomal rearrangement, limiting efficacy evaluation in each of these groups separately, the authors concluded that PGT-A/-SR may improve pregnancy rates per ET and reduce miscarriage rates per pregnancy when the individual has a history of RIF, RPL, or chromosomal rearrangement, especially in cases of advanced maternal age. However, euploid blastocysts cannot be retrieved in 60% or more of retrieval cycles, and it is not clear whether PGT-A/-SR improves the cumulative live birth rate (CLBR) per retrieval cycle or intention to treat (ITT). Further research that includes control groups and live birth rate (LBR) is needed to validate these results.

In a 2021 systematic review and meta-analysis, Hou et al. evaluated the risk of obstetric and neonatal adverse outcomes related to PGT. Those included were 785,445 individuals from 19 studies, who were separated into an IVF/ICSI group (n = 731,151) and a PGT group (n = 54,924). The outcomes included mean birth weight, LBW, very low birth weight, mean gestational age at birth, PTB, very preterm birth, intrauterine growth retardation (IUGR), birth defects, sex ratio, hypertensive disorders of pregnancy, cesarean section, gestational diabetes, disorders of the placenta, and preterm premature rupture of membranes. The analysis showed that pregnancies following PGT had reduced rates of LBW [risk ratio (RR), 0.85; 95% CI, 0.75-0.98], very low birth rates (RR, 0.52; 95% CI, 0.33-0.81), and very preterm births (RR, 0.55; 95% CI, 0.42-0.70) compared with these rates in the pregnancies following IVF/ICSI but higher rates of hypertensive

disorders of pregnancy (RR, 1.30; 95% CI, 1.08-1.57). PGT was not associated with a higher risk of any of the other adverse outcomes. In a subgroup analysis of blastocyte biopsies only, PGT using blastocyte biopsy yielded a lower rate of very low birth weight (RR, 0.55; 95% CI, 0.31-0.95) and was not associated with an increased risk of other obstetric/neonatal outcomes. A subgroup analysis was also undertaken for frozen-thawed ET cycles and indicated that pregnancies with PGT were associated with a lower rate of very low birth weight and cesarean birth but a higher rate of IUGR and PTB compared with the IVF/ICSI group; no other elevated risk was identified for frozen-thawed ETs. The authors concluded that based on the pooled analysis, PGT did not lead to an increase in the risk of adverse obstetric and neonatal outcomes; however, the association between PGT and an elevated risk of IUGR will require further investigation. The analysis is limited by the differences in the stage of embryo biopsy (cleavage stage vs blastocyst stage) and lack of studies that included obstetric indicators, such as placental disorders. In addition, none of the studies that were included were RCTs, which reduced the value of the meta-analysis. The researchers suggested ongoing analysis, with potential inclusion of spontaneously conceived (SC) pregnancies as a control group, to help further determine the safety and efficacy of PGT/embryo biopsy. The study by Li et al. (2021), previously discussed in this policy, was included in this systematic review.

Zheng et al. (2021; included in the Mao et al. meta-analysis discussed above) published a systematic review and meta-analysis that evaluated the outcomes of pregnancies in which an embryonic biopsy with PGT was performed compared with those of SC pregnancies or pregnancies conceived after IVF/ICSI. Overall, 15 studies, which included 3,682 babies born from pregnancies following PGT, 127,719 babies born from pregnancies following IVF/ICSI, and 915,222 babies born from SC pregnancies, were analyzed. The primary outcomes of the study included LBW and CMs. The secondary outcomes included preterm delivery, very preterm delivery, gestational age, birth weight, very low birth weight, neonatal intensive care unit admission, hypertensive disorders of pregnancy, gestational diabetes, placenta previa, and preterm rupture of membranes. Subgroups undergoing analyses included preimplantation genetic diagnosis (PGD), preimplantation genetic screening (PGS), cleavage stage biopsy in conjunction with fresh ET, and blastocyst biopsy in conjunction with frozen-thawed ET. The study findings indicate that the RR for LBW was higher in pregnancies following PGT compared with SC pregnancies (RR, 3.95; 95% CI, 2.32-6.72); however, there was no difference in the risk of CMs. The LBW and CM pooled results showed a similar risk in pregnancies following PGT and IVF/ICSI. For preterm delivery and hypertensive disorders of pregnancy, the risks were significantly higher in pregnancies following PGT compared with SC pregnancies (RR, 3.12, 95% CI, 2.67-3.64 and RR, 3.12, 95% CI, 2.18-4.47, respectively). In addition, lower gestational age (mean difference, -0.76 weeks; 95% CI, -1.17 to -0.34 weeks) and birth weight (mean difference, -163.80 g; 95% CI, -299.35 to -28.24 g) were found for pregnancies following PGT vs SC pregnancies. However, compared with pregnancies following IVF/ICSI, the risk of very preterm delivery and very low birth weight was significantly decreased in pregnancies following PGT (41% and 30%, respectively). Lastly, the risk of hypertensive disorders of pregnancy was 50% higher in pregnancies following PGT compared with pregnancies following IVF/ICSI. The additional subgroup analyses found that both pregnancies following PGD and PGS were associated with a higher risk of preterm delivery and a lower gestational age than SC pregnancies. The authors concluded that overall, their meta-analysis indicates that pregnancies following PGT may be associated with an increased risk of LBW, preterm delivery, and hypertensive disorders of pregnancy compared with SC pregnancies. When compared with pregnancies following IVF/ICSI, obstetric and neonatal outcomes appear to be favorable, although pregnancies following PGT were associated with a higher risk of hypertensive disorders of pregnancy. Limitations include the potential for bias related to merging data from RCTs and non-RCTs, limited available data, and variations in the populations studied. The authors recommended further studies, including RCTs and prospective cohorts, to confirm these findings.

In 2016, Chang and colleagues published a review of the outcomes of IVF using PGT from 2011 to 2012 from the United States Assisted Reproductive Technology Surveillance Data. Overall, they included 97,069 non-PGT cycles and 9,833 cycles that used PGT in their analysis. Most were for aneuploidy screening (55.6%), 29% were for other reasons, and 15% were for preventing genetic disease. In the “other reasons” category, only 2% of clinics provided information on the reason for PGT, and it was primarily for gender selection. In 2011, 98% of clinics reported doing at least one PGT cycle, and in 2012, 100% of reporting clinics had performed PGT cycles. The clinical characteristics between the three groups differed. The aneuploidy screening group tended to be older (aged > 37 years) and had a higher rate of prior miscarriages. As a group, they had fewer miscarriages than other age-matched groups in the study and had a higher chance of a live birth than the age-matched non-PGT group. They were more likely to have multiple births compared with the non-PGT group. This group was also more likely to have LBW babies. The genetic disease group was younger and did not have a history of prior miscarriages. In this group, in women aged 35 to 37 years, the adjusted odds of achieving a pregnancy and live birth were lower than that in the non-PGT group. In all categories, women using PGT who were less than 35 years old and transferred one embryo had odds of clinical pregnancy and live birth lower than that in the non-PGT group. Information was not available on the PGT techniques used by the different clinics, biopsy type, protocol to select chromosome abnormalities, number of embryos, embryo morphology, and/or number of embryos discarded. The authors concluded that PGT might improve outcomes in populations at risk of a genetically affected child, including aneuploidy, on

the basis of family history, but additional data collection and outcome data are necessary to better understand the overall value and effectiveness of PGT. Prospective, randomized studies are needed.

Preimplantation Genetic Testing for Monogenic/Single-Gene Defects

In a 2025 systematic review of observational studies, Poulton et al. summarized clinical pregnancy and LBR outcomes following PGT for monogenic/single-gene defects (PGT-M). An additional subgroup analysis of clinical outcomes of concurrent PGT-M and PGT-A was also performed. A total of 51 studies met the inclusion criteria for the review. Pooled data included 5,305 stimulated cycles and 5,229 ETs, which resulted in 1,806 clinical pregnancies and 1,577 live births. The clinical pregnancy rate was 34% (95% CI, 32.8%-35.3%), and the LBR was 29.7% (95% CI, 28.5%-31.0%) per cycle and 24.8% (95% CI, 23.6%-26.0%) and 21.7% (95% CI, 20.8%-23.1%) per ET, respectively, with noted significant statistical heterogeneity, which may be due to the variations in clinical populations, clinical practices, and date ranges of studies (more recent studies showed better outcomes). Based on these results, the authors asserted that clinical pregnancy and LBRs after PGT-M are better than those in women undergoing IVF for other indications. In the subgroup analysis in individuals receiving PGT-A concurrently with PGT-M, clinical pregnancy and LBRs were 43.3% and 37.6% per cycle and 37% and 31.8% per ET, whereas studies without aneuploidy screening reported clinical pregnancy and LBRs of 32.5% and 28.1% per cycle and 21.2% and 18.6% per ET. There was a significant association between the use of concurrent aneuploidy screening and improved clinical outcomes when outcomes were stratified according to the monogenic inheritance pattern, across all domains, except the recessive LBR per cycle. Although these results are limited by varied levels of quality and clarity in the included studies as well as the age of the studies reviewed (over one-third were published more than 10 years ago), the researchers suggested that their systematic review results offer promising data for individuals in whom PGT-M is indicated and will also help provide a stronger evidence base for genetic counseling as well.

In a Cochrane systematic review, Vlajkovic et al. (2022) sought to investigate the benefits and/or harms of biopsies performed on day 3 of embryo development compared with those of biopsies performed on day 5 in individuals undergoing PGT-M with IVF or ICSI cycles. Only one small RCT was found, which included 20 individuals, and there was a risk of bias due to a low level of precision and lack of blinding of study personnel. Based on the limited data available, there is uncertainty regarding whether there is a difference in live births and miscarriages, ectopic pregnancies, stillbirths, termination of pregnancy, and viable intrauterine pregnancies between embryos biopsied on day 3 and day 5 for PGT-M. Further studies are needed to confirm what impacts may exist for biopsies performed on either day 3 or 5 of embryo development.

Ben-Nagi et al. (2019) conducted an observational study to determine if LBR is affected by oocyte yield as well as the number of blastocysts biopsied and/or the number of acceptable blastocysts to transfer post PGT-M or PGT-SR. Participants were 175 couples who were referred to an IVF center from 2014 to 2017 and chose to undergo either PGT-M or PGT-SR. Overall, 145 couples (83%) had PGT-M, while 30 (17%) had PGT-SR. In total, 44 couples (25%) had second or third cycles of IVF, for a total of 249 oocyte retrievals and 230 frozen ETs (FETs); 196 (79%) were due to single-gene disorders, and 53 (21%) were due to chromosomal rearrangement. Overall, 122 (53%) of the FETs resulted in live birth, 16 (7%) resulted in ongoing pregnancy, 21 (9%) resulted in miscarriage, and 69 (30%) resulted in failed implantation. The authors found that the number of oocytes collected ($p = 0.007$; OR, 1.06), the number of blastocysts biopsied ($p = 0.001$; OR, 1.14), and the number of suitable embryos to transfer ($p = 0.00$; OR, 1.38) were all positively associated with achieving a live birth. The likelihood of live birth increased by 14% per additional blastocyst biopsied and by 38% per suitable embryo to transfer. A stratified analysis determined that the odds of live birth per acceptable embryo for transfer were 1.28 for single-gene disorders and 3.23 for chromosomal rearrangement.

Kubikova et al. (2018) reported on the development of a multiplex polymerase chain reaction (PCR) test for PGT-M of the β-globin gene (*HBB*), which is responsible for β-thalassemia and sickle cell anemia. The analysis used the amplification of overlapping small *HBB* segments to cover the entire gene, with analysis using next-generation sequencing (NGS). In addition, 17 closely linked single-nucleotide polymorphisms (SNPs) were tested simultaneously to aid in defining haplotypes, in combination with *HBB* sequencing. A validation study in five family trios, representing 14 different mutations, was conducted, and the results were consistent with previously obtained genetic results. Three of the families continued to use this protocol for PGT-M. One couple had a single-cell embryo biopsy at an early cleavage stage, and the other two families had approximately five cells extracted from the TE from blastocyst stage embryos. In total, 21 embryos were tested and had successful whole-genome amplification, and the NGS analysis was successful. Typical karyotyping and linkage analysis were performed simultaneously as a comparison for standard PGT methods. All but one embryo had an average read depth of 1,000 × for *HBB*. The single embryo that failed was found to have nullisomy for chromosome 11, where the *HBB* gene is located. In one couple, there were low call rates and a high allele dropout rate in the standard karyotype method, which were likely associated with suboptimal amplification after blastocyst biopsy. The results were resolved using a linkage analysis of parental SNPs to confirm mutations and haplotypes found in the embryos. The allele dropout was not found in the NGS analysis. The authors concluded that the use of a TE biopsy with NGS provided better

accuracy than traditional PGT testing. Pregnancy rates, outcomes, and confirmation of PGT results postnatally were not reported in this study.

Volozonoka et al. (2018) examined the difference between multiple displacement amplification (MDA) and OmniPlex whole-genome amplification when used for comparative genomic hybridization (CGH), Sanger sequencing, SNaPshot (single-base extension sequencing), and fragment size analysis. Nine couples at risk for single-gene disorders consented to participate in the study. The disease genes that were involved included *ACTA2, HTT, KRT14, ALOX12B, TPP1, GLB1, MTM1*, and *DMD*. A total of 62 embryos were tested, and one to eight trophectodermal cells were taken from the outer layer. All embryos survived the extraction. Overall, 39 embryos underwent whole-genome amplification using MDA, and the remaining went through OmniPlex linear amplification. Amplification detection was determined by capillary electrophoresis. Direct mutation analysis used Sanger sequencing or SNaPshot, and chromosomes were analyzed using CGH. Whole-genome amplification, regardless of method, and testing were successful and provided a conclusive result in all embryos. Five unaffected and euploid embryos were transferred, resulting in four clinical pregnancies and the live birth of two healthy children. However, key differences were noted. The MDA approach to whole-genome amplification resulted in heavier DNA strings; additionally, the resulting electrograms were clearer, and the base error rate was lower than that with other PCR-based approaches. MDA had significant amplification bias that caused high CGH noise. The authors concluded that methodology choice should depend on which downstream analysis is most needed, and both amplification techniques could be used if there are enough embryonic cells available.

Preimplantation Genetic Testing for Chromosomal Structural Rearrangements

Liu et al. (2024) conducted a study in 15 couples with unique complex chromosome rearrangements (CCRs); participants were retrospectively selected from 793 couples, who had undergone PGT-SR, to evaluate the clinical outcomes and influencing factors of PGT-SR in couples who were CCR carriers. In this study, one partner in each couple was a CCR carrier; five were female and 10 were male heterozygotes. More than half of the female participants had experienced abnormal pregnancy outcomes, including spontaneous or induced abortions. Oligoasthenoteratozoospermia was diagnosed in three of the male carriers, and the remainder had normal sperm parameters. The CCR carrier types were categorized into three groups: three-way rearrangements (A), double two-way translocations (B), and exceptional CCR (C). None of these couples had achieved a healthy live birth before undergoing PGT-SR. Overall, 100 blastocysts were biopsied, and all the 100 biopsied blastocysts were diagnosed successfully, with 16.0% identified as balanced or normal, 79.0% as aneuploid, and 5.0% as mosaic. Overall, 26 of the embryos showed de novo chromosomal abnormalities that were not present in the carriers. There were no statistically significant differences noted in the rate of euploid blastocysts across groups A, B, and C. Eleven normal/balanced embryos and one mosaic embryo were transferred and resulted in eight live births [LBR: 63.6% for euploid (seven of 11) and 100% (one of one) for mosaic embryos]. The authors also performed a systematic analysis, seeking to pinpoint factors that influence outcomes of PGT-SR in parents with CCR by integrating this study's outcomes with an additional 39 previously reported cases of balanced CCR and 352 successfully tested embryos. These results showed that the overall proportion of euploid embryos was 10.8%, with the rates in female participants who were aged < 35 and ≥ 35 years at 10.7% and 14.3%, respectively. After completing the multivariate generalized estimating equation analysis, type B CCRs and female carriers were identified as independent risk factors for fewer euploid embryos. Based on these data, the researchers suggested that the rate of balanced CCR in individuals with reproductive abnormalities may be higher than expected. Although the proportion of normal/balanced embryos was significantly low, PGT-SR may improve reproductive outcomes in individuals with CCR and assist with more comprehensive genetic counseling and clinical management.

In a 2022 retrospective analysis, Nakano et al. sought to assess the effectiveness of PGT-SR using array CGH (aCGH) or NGS in the prevention of recurrent miscarriage. The evaluation included 31 couples who had balanced translocations and had undergone a total of 68 PGT-SR cycles between 2012 and 2020. In all, 242 blastocytes underwent biopsy for aCGH or NGS, and the blastocysts that were identified as genetically transferrable were transferred in the subsequent frozen-thawed single ET cycle. The study found a genetically transferable rate of 21.2%, with 35 blastocysts transferred to the uterus. The rate of clinical pregnancy was 57.1%, and the OPR was 100%. The authors concluded that their results support the use of PGT-SR using aCGH or NGS to evaluate chromosomes and ultimately help prevent recurrent miscarriages. In addition, the results may be helpful in genetic counseling for carriers of balanced translocations.

Huang et al. (2019a) performed a retrospective cohort study in 194 couples with reciprocal translocation who had experienced two or more adverse pregnancy histories. Overall, 265 PGT-SR cycles were examined to assess the impact of PGT-SR on normal live birth, birth defect, and miscarriage rates in reciprocal translocation carrier couples. Prior to PGT-SR, the reproductive history of the couples consisted of 592 pregnancies; 83.6% resulted in miscarriages, 6.1% resulted in live birth with defects, 4.9% were terminated due to unwanted pregnancy, and 2.9% resulted in normal live births. Post PGT-SR, 118 clinical pregnancies resulted in 85.6% with normal live births, 11% with miscarriage, and 3.4% with birth defects. The authors concluded that reciprocal translocation carriers in this study had a low risk of miscarriage and birth defects and a higher frequency of normal live births following PGT-SR.

Zhou et al. (2018a) examined the validity of using massively parallel sequencing (MPS) on TE samples for PGT in chromosome translocation carriers. Twelve couples, who had chromosome translocations, participated in the study. Nine had balanced translocations, and three were carriers of a numerical chromosome abnormality. In total, 105 embryos were biopsied on day 3 and had one cell removed. The cells underwent whole-genome amplification and were tested for genomic imbalances using MPS and CGH, which were then confirmed using routine karyotyping. The results were obtained for MPS and CGH for 101 embryos, and there was concordance between MPS and CGH for 19 euploid and 82 unbalanced or aneuploidy embryos. However, there were four discrepancies. In one blastomere, MPS found a deletion of an X chromosome that was not found by CGH. This may have been caused by a low density of SNPs on the CGH platform in that region. In another case, MPS identified a 186-Mbp duplication on chromosome 1 and a 15.6-Mbp duplication on chromosome 5, whereas CGH identified the duplications but of a different size. This could be related to amplification bias that impacts CGH that would have been corrected in the MPS bioinformatics process. In the third embryo, karyotyping and MPS identified an unbalanced translocation between chromosomes 3 and 6, and CGH only identified the imbalance in chromosome 3. In the final discrepant embryo, karyotype and MPS identified an unbalanced translocation between chromosomes 13 and 22, and CGH only identified the imbalance in chromosome 13. Twelve of the 19 embryos that were found to be free of genomic imbalances were used for frozen-thaw ET, resulting in one live birth and five ongoing pregnancies.

Segmental mosaicism is a concern with both PGT-A and PGT-SR. Zhou et al. (2018b) examined the frequency of de novo segmental aneuploidy identified by NGS. The study took place over a 3-year time period and involved 5,735 blastocysts from 1,854 couples who underwent PGT-A (n = 770) and PGT-SR (n = 1,084) on TE biopsies. Biopsied cells had whole-genome amplification using GenomePlex amplification and low-coverage MPS on the Proton platform. Overall, 581 blastocysts were found to have 782 de novo segmental aneuploidies. Most carried only one, but 115 had two; 38 had three or more. There was no association with advanced maternal age or a specific chromosome. In 1,377 cycles, 1,686 blastocysts were transferred, resulting in clinical pregnancies in 49% of the PGT-SR group and 47% of the PGT-A group. The miscarriage rate was approximately 9% in both groups. At the time of publication, there were 84 prenatal diagnostic tests and 645 delivered babies who were considered normal and healthy. Overall, 40 blastocysts with de novo segmental aneuploidy were donated for further research and were additionally analyzed by fluorescence in situ hybridization (FISH) as a comparison analysis. Of the donated blastocysts, 39 were successfully analyzed, and FISH confirmed the segmental aneuploidy identified by NGS. Because de novo segmental aneuploidy can be caused by either meiosis during gamete formation or during mitosis during embryo development, the TE and inner cell mass were evaluated for 26 blastocysts. Five showed pure segmental mosaicism in both the TE and inner cell mass, but 14 showed different levels of mosaicism between the two tissue types. The authors concluded that this analysis revealed that segmental de novo aneuploidy is a real issue and is not an artifact of whole-genome amplification. Further studies are needed to understand de novo segmental mosaicism and its impact on embryo development.

Maithripala et al. (2018) reviewed the reproductive choices of 36 couples who experienced recurrent miscarriage as a result of one member of the couple carrying a balanced chromosome translocation. The couples were identified through a retrospective chart review of 2,321 couples seen in a highly specialized reproductive assistance clinic between 2005 and 2013. The prediagnosis obstetric history was obtained, and it was similar for all couples. The date of parental diagnosis was identified for each couple and used in determining the time from diagnosis to live birth as a point of comparison between couples who chose natural conception and those who picked PGD as their reproductive choice. Overall, 23 couples chose to pursue natural conception, and 13 chose PGT-SR. In the natural conception group, there were 24 live births, with a live birth incidence of one birth per 4.09 years, and 74% of women had at least one live birth in the follow-up period. In the PGT-SR group, six live births were recorded, reflecting a live birth incidence of one birth per 5.63 years, and 38% of women had at least one live birth in the follow-up period. There was no significant difference between the groups in postparental diagnosis, miscarriage, or LBRs. It should be noted that in the PGT-SR group, the miscarriage rate did not take into consideration PGT-SR–specific variables. There were eight failed PGT-SR cycles, which included four euploid ETs that did not result in pregnancy. While failed PGT-SR and miscarriage cannot be equated, the authors felt that it was meaningful to report, as cycle failure represents a significant effort that results in failure to achieve live birth.

Iews et al. (2018) conducted a systematic review of the literature to examine the evidence supporting the use of PGT-SR in couples who have experienced recurrent miscarriages due to an inherited structural chromosome rearrangement. A meta-analysis was not possible because of significant differences between the studies. The authors identified 20 studies after a comprehensive review of the literature. Live birth was the primary outcome that was analyzed, and the secondary outcomes reviewed included miscarriage rate and time to successful pregnancy. A pooled total of 847 couples who conceived naturally had an LBR of 25% to 71%. A pooled total of 562 couples had PGT-SR, and they had a similar LBR of 26% to 87%. There were no large comparative or randomized studies found. The studies also had different inclusion criteria, and some evaluated individuals for additional causes of miscarriage, such as autoimmune disease, whereas others did not. Some studies found a lower miscarriage rate in the PGT-SR group, and others did not. Two studies were identified as the best comparative analysis for examining the miscarriage rate and time to live birth post parental

diagnosis, and the studies had conflicting results. One found a lower miscarriage rate in the PGD group, and the other did not. Both found a similar time to LBR for PGT-SR and natural conception.

The ability of NGS to detect CCRs compared with CGH was the focus of a study by Chow et al. (2018). The authors used archived whole-genome amplified DNA from 342 embryos at risk of genomic imbalance because of translocation or inversion carrier parents. All embryos had been previously analyzed by CGH. There were 287 blastomere biopsies and 55 TE biopsies. Overall, the concordance rate on abnormal results was 100% between NGS and CGH, regardless of the biopsy type. The concordance in normal embryos was 98% in the blastomere biopsy group and 79% in TE biopsies. NGS detected de novo segmental aneuploidy and low-level mosaicisms that were not identified by CGH. The authors concluded that NGS is an acceptable technology to use in PGT-SR.

Preimplantation Genetic Testing for Human Leukocyte Antigen Typing

A collaborative multicenter study by Kakourou et al. (2018), with the support of the European Society of Human Reproduction and Embryology (ESHRE), focused on the diagnostic and clinical efficacy of PGD for human leukocyte antigen (PGD-HLA) potential positive outcomes. A total of 14 centers submitted data through a custom database from 716 PGD-HLA cycles; of these, 704 cycles from 364 couples met the inclusion criteria. The mean maternal age was 33.5 years, and 81.3% of the couples who were tested had requested HLA typing without concurrent exclusion of single monogenic disease (58.63% β-thalassemia). Overall, 9,751 oocytes were obtained, and 5,532 embryos underwent analysis. Cycles predominantly used fresh oocytes (94.9%) with day 3 biopsy (85.3%). A diagnosis was made in 4,343 embryos (78.5%); of these, 677 were found to be genetically suitable. Subsequently, 56.6% of the 364 couples underwent ET, and 598 total embryos were transferred (382 cycles). Ultimately, human chorionic gonadotropin–positive pregnancies were obtained in 164 couples, and 136 babies were born to 113 couples. Limitations to the overall success of the procedure include maternal age, number of oocytes collected per cycle, and genetic chance. In 57 cases, hematopoietic stem cell transplant was reported; 64.9% used combined umbilical cord blood and bone marrow transplant, and 77% of transplants identified no complications. In this study, the diagnostic efficacy (78.5%) was noted to be lower than the data previously reported for general PGD by ESHRE (92.6%). The pregnancy rate was 23.3% compared with the previously reported 25%. However, when ET was completed, the LBR and ET data were comparable between this study (34.3%) and existing ESHRE PGD data (34%). Diagnostic efficacy was also lower in this study than that reported in other PGD-HLA sources (78.5% vs 89.5%-94.1%). The study was limited by the use of retrospective data collection from facilities with varying practices and strategies for ART as well as the potential reporting bias when using the online database. This was the first multicenter study that analyzed the clinical utility of PGD-HLA over 15 years, and important parameters for more positive end points were brought to light. The authors indicated that the study reinforces the need for high-level collaboration of all specialists involved in ART, including PGD-HLA testing, and the need for ongoing data collection. They noted that published systematic data on methodology, clinical and diagnostic results, and the success rates of ART and hematopoietic stem cell transplant remain limited at this time.

Preimplantation Genetic Testing for Aneuploidy Screening

There is insufficient evidence to support the use of PGT for aneuploidy screening at this time. Findings from higher-quality studies are conflicting. Further studies that are focused on clinical utility and the development of algorithms to identify populations in which this testing may be beneficial are needed.

Beebeejaun et al. (2025) conducted a pilot RCT to evaluate the feasibility and clinical impact of PGT-A vs those of conventional morphology-based embryo selection in 100 women who were aged 35 to 42 years, which is a population at higher risk for embryonic chromosomal abnormalities. The trial addressed the persistent uncertainty regarding whether PGT-A meaningfully improves reproductive outcomes in older individuals; this is an age group that is underrepresented in prior randomized studies. Among embryos biopsied in the PGT-A arm, 51.4% were euploid, and 6.6% were low-level mosaic, reflecting the high level of aneuploidy in this age group. The clinical outcomes were similar between groups (PGT-A vs control), with clinical pregnancy rates of 50% vs 40%, LBRs of 50% vs 38%, and miscarriage rates of 12% vs 8%, respectively; however, the PGT-A group had a nonsignificant trend toward a higher cumulative LBR after up to three transfers (72% vs 52%) and required fewer transfers to conceive. The authors noted several limitations, including the small pilot sample, which diminished statistical power; single-center design, which reduced generalizability; unblinded participants and clinicians, which introduced potential bias; and limited ability to fully evaluate outcomes for mosaic embryos. Overall, the study demonstrated feasibility while highlighting the need for larger multicenter trials to determine whether PGT-A provides a truly meaningful clinical benefit in older women.

Bulletti et al. (2025) performed a systematic review and meta-analysis to evaluate the impact of embryonic and extraembryonic factors on embryo implantation success in ARTs, focusing on euploid vs untested ETs, age-related outcomes, and the role of gestational carriers. The study included 11 clinical trials and registry data from multiple countries, analyzing outcomes such as implantation and LBRs. PGT-A significantly improved implantation odds,

particularly in younger individuals, while older age was associated with reduced implantation, even in gestational carrier cycles. Gestational carriers consistently had higher implantation and LBRs than noncarriers, highlighting a secondary but notable role of extraembryonic factors. The authors concluded that embryo euploidy is the primary determinant of implantation success, with extraembryonic influences such as uterine environment and age-related endometrial changes playing a lesser but relevant role. They recommended focusing on PGT-A, optimizing endometrial receptivity, and considering gestational carriers in cases of RIF. The small number of included studies (n = 11), observational designs, and heterogeneity in study designs and populations limit the confidence in the findings, and authors disclosed funding from Merck.

Mumusoglu et al. (2025) conducted a systematic review and meta-analysis to assess the utility of PGT-A in managing unexplained RPL. Studies that involved individuals with two or more spontaneous pregnancy losses who underwent ART, with or without PGT-A, were included, and the primary outcome assessed was LBR. Rates of aneuploidy, clinical pregnancy, and clinical pregnancy loss were also evaluated. After the exclusion criteria were applied, 18 studies were incorporated in this evaluation. The meta-analysis indicated that the transfer of euploid blastocysts led to comparable pregnancy loss rates and LBRs in individuals with or without unexplained RPL (OR, 1.10, 95% CI, 0.57-2.13 and OR, 1.04, 95% CI, 0.74-1.44, respectively). Additionally, chromosome analysis of products of conception showed similar rates of aneuploidy among individuals with or without RPL. The use of PGT-A reduced the clinical pregnancy loss rate (OR, 0.42; 95% CI, 0.27-0.67) while improving the LBR per transfer (OR, 2.17; 95% CI, 1.77-2.65) and per individual (OR, 1.85; 95% CI, 1.18-2.91) in those with unexplained RPL. The authors speculate that individuals with adequate ovarian reserve undergoing ART may find PGT-A to be beneficial because it potentially increases the number of gametes available for conception, which could reduce the time to live birth. Although this study yielded promising results for individuals with unexplained RPL, further high-quality RCTs that compare ART, including PGT-A, with standard management for unexplained RPL are needed.

Cai et al. (2025) used a retrospective observational cohort study to evaluate whether PGT-A on previously cryopreserved unbiopsied blastocysts improves pregnancy outcomes in patients with a history of two or more clinical pregnancy losses, including at least one following IVF. Conducted at a single tertiary fertility center in China between 2016 and 2023, the study included 146 patients; 72 underwent PGT-A on thawed blastocysts (274 blastocysts), and 74 proceeded directly to FET without PGT-A (107 blastocysts). The primary outcome was the cumulative live birth rate or OPR. The PGT-A group had a significantly lower cumulative live birth rate/OPR than the non–PGT-A group. The secondary outcomes, including live birth and pregnancy loss rates after the initial FET, were similar between groups. Among tested blastocysts, the euploidy rate was 48.6%, and 82.9% of patients had at least one euploid embryo. The study concluded that PGT-A on cryopreserved unbiopsied blastocysts did not improve and may reduce cumulative pregnancy outcomes in this population. The results may be affected by selection bias, given that patients in the PGT-A group had more prior aneuploid losses. The limited sample size suggests vulnerability to type II errors (false-negative findings).

Adamyan et al. (2024) conducted a systematic review and meta-analysis to evaluate the effectiveness of PGT-A in IVF/ICSI cycles across different age groups and prognostic profiles. Overall, 19 clinical trials (five randomized and 14 nonrandomized) that involved approximately 100,000 IVF cycles were included, with studies selected based on the use of aCGH or NGS for PGT-A. In individuals aged > 35 years, PGT-A significantly improved the clinical pregnancy rate per ET and LBR per individual. In individuals aged ≤ 35 years, PGT-A was associated with a higher LBR per ET, but no significant differences were found in miscarriage rates or LBR per individual. Among individuals with poor prognosis, including those with RPL or implantation failure, PGT-A significantly improved LBRs per ET. The authors concluded that PGT-A is effective in improving reproductive outcomes in older individuals and those with poor prognosis undergoing assisted reproduction, while its benefit in younger individuals remains unproven. The clinical trials included in the review were made up of both randomized and nonrandomized studies, with differences in outcome reporting (e.g., outcomes per ET vs outcomes per individual) and a mixture of fresh and FETs, any of which may confound the reported results. The publication by Yan et al. (2021), previously discussed in this policy, was included in this systematic review and meta-analysis.

Mei et al. (2024) conducted a systematic review to evaluate the impact of PGT-A on reproductive outcomes in individuals with recurrent reproductive failure, including RPL and RIF. The review included 20 studies published between 2014 and 2023 and comprised two prospective and 18 retrospective studies. The studies showed that PGT-A improved LBRs and clinical pregnancy rates and reduced miscarriage rates in individuals with recurrent reproductive failure, particularly in those of advanced maternal age. However, the benefits of PGT-A were limited in individuals with multiple prior pregnancy losses or poor ovarian reserve. The review concluded that while PGT-A can optimize reproductive outcomes in recurrent reproductive failure, especially in older individuals, its effectiveness may be reduced in cases with repeated failures or diminished ovarian response, and further large-scale RCTs are needed to identify the populations that benefit most. A meta-analysis was forgone due to the studies' heterogeneity and inconsistent outcome definitions, which reduces the ability to quantify effect sizes.

Another systematic review and meta-analysis (Taskin et al., 2024) evaluated the impact of PGT-A on IVF outcomes. Seven RCTs, which included 1,851 individuals, were analyzed and compared IVF with PGT-A (via polar body, day 3, or TE biopsy) with IVF without PGT-A. The primary outcome was the OPR, with secondary outcomes including clinical pregnancy rate and miscarriage rate. The meta-analysis found no significant improvement in OPR or clinical pregnancy rate with PGT-A in all age groups, including subgroups of individuals who were < 35 and ≥ 35 years old. However, PGT-A was associated with a significantly lower miscarriage rate in the all-ages group, although this effect was not significant when stratified by age. The authors concluded that PGT-A does not improve pregnancy rates but may reduce miscarriage rates and emphasized the need for further standardized trials to determine the true clinical value of PGT-A. Strict reliance on RCTs enhances internal validity but also provides small sample sizes in subgroups, especially where there is heterogeneity in biopsy timing and testing methods or methodological flaws in the included studies. The publication by Verpoest et al. (2018), previously discussed in this policy, was included in this systematic review and meta-analysis.

To investigate whether individuals with recurrent pregnancy failure (RPF), who had undergone PGT-A, achieved better clinical outcomes than those who did not have PGT-A, Liang et al. (2023) performed a systematic review and meta-analysis of 13 studies; 930 individuals in whom PGT-A had been performed and at least 1,434 individuals who did not receive this testing were included. In the PGT-A group, 1,015 ETs were completed. In the group that did not have PGT-A, 1,799 embryos were transferred successfully. The analysis yielded evidence of superior clinical outcomes in the PGT-A group, with improvements in implantation rate (RR, 2.01; 95% CI, 1.73-2.34), clinical pregnancy rate (RR, 1.53; 95% CI, 1.36-1.71), OPR (RR, 1.76; 95% CI, 1.35-2.29), and LBR (RR, 1.75; 95% CI, 1.51-2.03). The PGT-A group also had a significantly lower rate of miscarriage (RR, 0.74; 95% CI, 0.54-0.99). In a subgroup analysis focused on age, PGT-A resulted in better clinical pregnancy rates and LBRs in individuals both under the age of 35 years and those aged 35 years or older compared with individuals who did not have PGT-A ($p < 0.01$ and $p < 0.05$, respectively). The researchers asserted that their findings strengthen the evidence for the use of PGT-A in individuals with RPF. Several limitations were noted, including the small number of studies included (especially for subgroup analyses) and the lack of comprehensive raw data. In addition, a high risk of bias related to the blinding of personnel and individuals in the included RCTs was noted. Further high-quality, controlled trials, with larger and more varied populations, are needed to support the use of PGT-A in individuals with RPF.

In a retrospective cohort study, Kucherov et al. (2023) analyzed the impact of PGT-A on CLBR when used in IVF cycles. Data from the SART CORS (Society for Assisted Reproductive Technology Clinic Outcome Reporting System), a national registry that includes over 85% of U.S. programs that perform IVF, were used to compare CLBR in patients using autologous oocytes, either with or without PGT-A. Donor oocyte cycles, donor embryo cycles, gestational carrier cycles, cycles that included both fresh ET and thawed embryo that had previously been frozen (ET plus FET), and cycles using fresh ET after PGT-A were excluded from the study. In all, 133,494 IVF cycles were evaluated. A decrease in CLBR was found in the PGT-A group across age groups, with the exception of patients over 40 years of age ($p < 0.01$). The researchers performed a subgroup analysis in only patients who had undergone FET subsequent to PGT-A (not including those in whom no embryos were transferable) and found a very high CLBR (ranging from 71.2% in patients less than 35 years old to 50.2% in patients over 42 years old). Of note, rates for PTB, early pregnancy loss, multiple gestations, and LBW were greater in the group that had not undergone PGT-A. The study was limited by its retrospective design, which impacted its use for demonstration of causal relationships, and it had missing and/or outlier data points. The researchers concluded that overall, in patients 40 years of age or younger with blastocysts available for ET or PGT-A, there was an association between PGT-A and decreased CLBR, which was notably higher in patients under 35 years of age. They further stated that PGT-A may show utility in individuals with advanced maternal age and may be associated with lower rates of miscarriage. For the most accurate individual outcome measure, the authors recommended the use of CLBR per cycle vs first transfer LBR when determining the utility of PGT-A. Lastly, the importance of counseling regarding the utility of PGT-A, based not only on maternal age but potential miscarriage benefit, was stressed.

In a 2022 systematic review and meta-analysis (Cheng et al.), pregnancy outcomes among individuals undergoing IVF, either with or without PGT-A, were compared. Nine RCTs, which included 3,334 individuals, were included in the review. The analysis found that PGT-A was not related to an increase in LBR overall (RR, 1.13; 95% CI, 0.96-1.34; $I^2 = 79\%$), but it was associated with an increase in the LBR in those with advanced maternal age (RR, 1.34; 95% CI, 1.02-1.77; $I^2 = 50\%$). In addition, PGT-A was related to a decreased miscarriage rate (RR, 0.53; 95% CI, 0.35-0.81; $I^2 = 50\%$). The primary limitation of the study is the high level of heterogeneity of the studies included ($p < 0.001$; $I^2 = 79\%$). A subgroup analysis identified age as the main factor leading to the high heterogeneity. Based on the study results, the authors posited that PGT-A increases LBR in individuals of advanced maternal age. The publications by Yan et al. (2021) and Verpoest et al. (2018), previously discussed in the evidence, were included in this systematic review.

The use of PGT-A in patients with RPL was the focus of a retrospective study performed by Bhatt et al. (2021; included in the Mumusoglu et al., 2025, systematic review and the Mei et al., 2024, systematic review); data from SART CORS were used. The researchers aimed to discern whether PGT-A was associated with improved LBRs in couples with RPL who

were undergoing IVF with FET. RPL was defined as a history of at least three pregnancy losses. In total, 12,631 FET cycles for 10,060 couples were analyzed, including 4,287 cycles in couples with a history of a tubal disease, who formed a control group. Couples with RPL undergoing FET, either with or without PGT-A, made up the experimental group. The primary outcome of this study was LBR. The rates of clinical pregnancy, spontaneous abortion, and biochemical pregnancy loss were secondary outcomes. The results indicated that in this large study, PGT-A was associated with an increase in LBR and clinical pregnancy in patients with RPL. The greatest difference was seen in patients who were older than 42 years. However, because this retrospective study included only patients with RPL undergoing FET, the results may not be generalizable to all those with RPL. In addition, the data regarding clinical evaluation and the treatments received for RPL for the patients included in the study were not obtainable. The authors encouraged counseling on all options for the management of RPL, which may include IVF with PGT-A for embryo selection to increase the chance of live birth, especially for those individuals with advanced maternal age.

Simopoulou et al. (2021) published a systematic review and meta-analysis of RCTs that focused on the identification of age group(s) that may benefit from PGT-A and the best day to perform a biopsy for the testing. A systematic literature search identified 11 RCTs that used PGT-A with comprehensive chromosomal screening on either day 3 or day 5 and met the eligibility criteria. After the analysis, the researchers found that PGT-A was not related to improved LBRs per individual in the overall population (RR, 1.11; 95% CI, 0.87-1.42; n = 1,513; I^2 = 75%), but it was associated with lower miscarriage rates (RR, 0.45; 95% CI, 0.25-0.80; n = 912; I^2 = 49%). Notably, PGT-A was associated with improved CLBR per individual (RR, 1.36; 95% CI, 1.13-1.64; n = 580; I^2 = 12%). In a subgroup analysis, PGT-A was associated with a higher LBR in individuals who were older than 35 years (RR, 1.29; 95% CI, 1.05-1.60; n = 692; I^2 = 0%), but it did not have this association for younger individuals (RR, 0.92; 95% CI, 0.62-1.39; n = 666; I^2 = 75%). In terms of timing, day 5 biopsies showed an improved LBR per ET (RR, 1.37; 95% CI, 1.03-1.82; I^2 = 72%). The authors concluded that while PGT-A did not appear to improve outcomes in the overall population, it was associated with improved LBRs when performed on blastocyst stage embryos in individuals over the age of 35 years. However, the number of studies included in the meta-analysis was relatively small, and the ages of most of the individuals included were not necessarily representative of individuals who commonly undergo PGT-A testing. The researchers encouraged further study to evaluate the characteristics of individuals who may benefit from PGT-A, with a focus on developing an algorithm to assist with decision-making regarding the appropriate population for PGT-A use.

In a 2021 publication, Tiegs et al. reported the outcome of their prospective, multicenter, blinded, nonselection study to evaluate the value of a diagnosis of aneuploidy (made via targeted NGS PGT-A) in predicting failure of a successful delivery. A secondary outcome that was measured was the impact of TE biopsy on lasting implantation. A total of 402 participants with infertility received 484 single, frozen blastocyst transfers. Results from unblinded PGT-A, performed using NextSeq 500/550 NGS-based PGT-A, were compared with the clinical outcomes of ETs, and a calculation of predictive values was made. A significant difference in outcome by PGT-A diagnosis was found; 64.7% (202 of 312) of euploid embryos progressed to either sustained implantation or delivery, while none of the 102 embryos that were diagnosed as whole-chromosome aneuploid progressed to either sustained implantation or delivery. Thus, the clinical error rate in aneuploid diagnoses was 0%. There was no difference in sustained implantation between the control group, which was age matched and had not undergone biopsy, and the PGT-A testing group. The authors asserted that the PGT-A assay that was evaluated was found to be prognostic of failure to deliver when such testing revealed an aneuploid result and did not result in the discard of embryos that had significant reproductive potential. However, they did note limitations, including the inability to analyze predictive values that were associated with segmental PGT-A or whole-chromosome mosaic diagnoses due to the low incidence of those results. Additionally, the retrospective identification of a control group to evaluate the impact of cell biopsy on sustained implantation limits the study's strength. Lastly, approximately half of the study participants were less than 35 years of age; however, the false-positive rates of aneuploidy are typically higher in this group than in older individuals, so this may have further challenged the accuracy of the assay used in this study. The researchers recommended that nonselection studies be performed for every new PGT-A assay as additional technologies emerge. This study was included in the Adamyan et al. (2024) systematic review, discussed above.

Konstantinidis et al. (2020) studied the incidence and patterns of trisomies and recombination separately and in conjunction with each other at the blastocyst stage by SNP testing with aCGH. SNP microarrays were performed on 1,442 blastocyst embryos from 268 couples who underwent PGT for known single-gene disorders; 24-chromosome aneuploidy screening by aCGH was done concurrently. Overall, 100% of meiotic trisomies were maternal in origin, and the incidence increased significantly with maternal age ($p < 0.0001$). Meiosis I trisomies and meiosis II trisomies were 55.8% and 44.2%, respectively. Recombination studies were performed for 11,476 chromosomes, and 17,763 recombination events were reported. The average number of recombination sites was 24.0 ±0.3 for male meiosis and 41.2 ±0.6 for autosomal female meiosis. In total, 190 euploid embryos and 69 embryos with maternal meiotic trisomies were compared, which revealed similar recombination rates ($p = 0.425$) and nonrecombinant chromatid rates ($p = 0.435$). Although the study

provided unique data regarding recombination and aneuploidies in embryos, further research and data are needed to establish clinical validity and clinical utility.

The effectiveness and safety of PGT-A was evaluated by Cornelisse et al. (2020), who performed a systematic review of six databases and two trial registries in September 2019. Thirteen RCTs, which involved 2,794 women and reported data on clinical outcomes in individuals who underwent IVF with PGT-A vs IVF without PGT-A, were included. The quality of evidence ranged from low to moderate. The CLBR was the primary outcome; the LBR after first ET, miscarriage rate, OPR, clinical pregnancy rate, multiple pregnancy rate, proportion of women obtaining an ET, and mean number of ETs represented the secondary outcomes. The authors reported that one trial used polar body biopsy with aCGH and stated that it is uncertain whether the addition of PGT-A by polar body biopsy increases the CLBR compared with IVF without PGT-A (OR, 1.05; 95% CI, 0.66-1.66; one RCT; n = 396; low-quality evidence). The evidence suggests that for the observed CLBR of 24% in the control group, the chance of live birth following the results of one IVF cycle with PGT-A is between 17% and 34%. It is uncertain whether the LBR after the first ET improves with PGT-A by polar body biopsy (OR, 1.10; 95% CI, 0.68-1.79; one RCT; n = 396; low-quality evidence). PGT-A with polar body biopsy may reduce the miscarriage rate (OR, 0.45; 95% CI, 0.23-0.88; one RCT; n = 396; low-quality evidence). No data on OPR were available. The effect of PGT-A by polar body biopsy on improving the clinical pregnancy rate is uncertain (OR, 0.77; 95% CI, 0.50-1.16; one RCT; n = 396; low-quality evidence). Another trial used blastocyst stage biopsy with NGS. It is uncertain whether IVF, with the addition of PGT-A by blastocyst stage biopsy, increases the CLBR compared with IVF without PGT-A, since no data were available. It is uncertain if LBR after the first ET improves with PGT-A with blastocyst stage biopsy (OR, 0.93; 95% CI, 0.69-1.27; one RCT; n = 661; low-quality evidence). It is uncertain whether PGT-A with blastocyst stage biopsy reduces the miscarriage rate (OR, 0.89; 95% CI, 0.52-1.54; one RCT; n = 661; low-quality evidence). No data on OPR or clinical pregnancy rate were available. For the comparison of IVF with PGT-A vs IVF without PGT-A, with the use of FISH for the genetic analysis, 11 trials were included. It is uncertain whether IVF with the addition of PGT-A increases the CLBR (OR, 0.59; 95% CI, 0.35-1.01; one RCT; n = 408; low-quality evidence). The evidence suggests that for the observed average CLBR of 29% in the control group, the chance of live birth following the results of one IVF cycle with PGT-A is between 12% and 29%. PGT-A, performed with FISH, probably reduces live births after the first transfer compared with the control group (OR, 0.62; 95% CI, 0.43-0.91; 10 RCTs; n = 1,680; I^2 = 54%; moderate-quality evidence). The evidence further suggests that for the observed average LBR per first transfer of 31% in the control group, the chance of live birth after the first ET with PGT-A is between 16% and 29%. There is probably little or no difference in miscarriage rate between PGT-A and the control group (OR, 1.03; 95%, CI, 0.75-1.41; 10 RCTs; n = 1,680; I^2 = 16%; moderate-quality evidence). The addition of PGT-A may reduce the OPR (OR, 0.68; 95% CI, 0.51-0.90; five RCTs; n = 1,121; I^2 = 60%; low-quality evidence) and probably reduces clinical pregnancies (OR, 0.60; 95% CI, 0.45-0.81; five RCTs; n = 1,131; I^2 = 0%; moderate-quality evidence). The authors concluded that due to the poor quality of evidence regarding CLBR, LBR after transfer, and miscarriage rate between IVF with and IVF without PGT-A, routine clinical practice of PGT-A is not supported.

TE biopsy, a technique to assess aneuploidy for PGT, can result in false-positive and false-negative test results because the chromosome number in TE cells is not always concordant with the chromosome number of the inner cell mass, which develops into the fetus. Huang et al. (2019b) conducted an investigational study to determine the effectiveness of noninvasive PGT for aneuploidy (niPGT-A) compared with that of the standard TE biopsy method. Overall, 52 frozen donated blastocysts were analyzed by NGS to serve as a gold standard. TE biopsy, PGT-A, and niPGT-A, results were generated for all samples and compared with sequencing results from corresponding embryos. The false-negative rate for niPGT-A was 0. The positive predictive value and specificity were higher for niPGT-A than for TE biopsy PGT-A. In addition, the authors stated that the concordance rates for embryo ploidy and chromosome copy number were also higher for niPGT-A than those for TE biopsy PGT-A. Based on this study, the authors concluded that niPGT-A by DNA sequencing of DNA released in culture media from both TE and inner cell mass provides a noninvasive method that is less prone to errors that are linked to embryo mosaicism, although future studies, with larger sample sizes, are necessary.

Munné et al. (2019; included in the Adamyan et al., 2024, and Taskin et al., 2024, systematic reviews discussed above) conducted a multicenter RCT [the STAR (Single Embryo Transfer of Euploid Embryo) study] to assess the benefit of PGT-A when used to select embryos for frozen-thawed ET. A total of 661 participants were included; participants were 25 to 40 years of age (average age, 33.7 ±3.6 years) and were undergoing IVF using autologous oocytes, with at least two blastocysts of adequate quality for biopsy and vitrification by day 6. Participants were enrolled from 34 clinics and tested in nine laboratories across the U.S., Canada, the U.K., and Australia. Overall, 330 participants were randomized to the arm of the trial using PGT-A for selection of embryos, and 331 were randomized to the control arm using morphology alone for embryo selection. Participants, physicians, and IVF clinical staff (not the embryologists) were blinded to the participants' randomization status. The primary outcome was the OPR at 20 weeks' gestation per ET. In the PGT-A group, 274 participants (83.0%) received the planned treatment, and in the control group, 313 (94.6%) received the planned treatment. Some randomized participants did not receive their planned treatment for various reasons, including lack of euploid embryos, withdrawal from the study, thaw failure, and deviation from the protocol. Noted was that the frequency of

the lack of euploid embryos increased with maternal age. After the analysis, the OPR was found to be comparable between the PGT-A group and the control group, with no significant difference found per ET [50% (137/274) vs 46% (143/313)] or per ITT at the time of randomization [41.8% (138/330) vs 43.5% (144/331)]. In addition, the rates of negative β-human chorionic gonadotropin, biochemical pregnancy, miscarriage, and elective termination per ET did not demonstrate significant differences between the study arms. A post hoc subgroup analysis showed a higher OPR in women who were aged 35 to 40 years after PGT-A [51% (62/122) vs 37% (54/145)] per ET but not per ITT. Ultimately, the authors concluded that PGT-A did not lead to improved overall pregnancy outcomes in all women in the study, whether evaluated per ET or ITT, but it does support the use of PGT-A in individuals who are 35 to 40 years of age to improve outcomes per frozen-thawed ET (although the improvement was not significant when analyzed per ITT). They were surprised that despite detecting a relatively high rate of aneuploidy in both the control and PGT-A arms of the study, PGT-A did not appear to improve the rate of implantation or OPR per ET in the younger participants. Since the IVF laboratory staff was not blinded to study participation or assigned group, it is possible that more embryos of lesser quality were biopsied and vitrified because of study participation that otherwise may have been discarded. This could have contributed to the failure to achieve a greater benefit of PGT-A and represents a potential limitation of the study. In addition, the targeted sample size of 300 transfers per study arm was not reached, primarily due to the lack of sufficient euploid embryos in the PGT-A arm, and there was no control of participant demographics; more than half of participants were younger than 35 years of age, which is considerably younger than is experienced in most fertility clinics. This trial highlighted the difficulties of large, multicenter RCTs in complex medical treatments such as IVF and underscored the importance of fully vetting novel diagnostics and laboratory procedures prior to implementation in standard clinical practice.

Zore et al. (2019) compared the outcomes of frozen SET between euploid embryos and those with segmental mosaicism. Overall, 327 women had 377 FETs. All embryos underwent biopsy at the blastocyst stage, during which two or more cells were taken from the TE. CGH was used to determine if embryos were euploid or had segmental mosaicism. In total, 357 were euploid, and 20 had segmental mosaicism. The spontaneous miscarriage rate was 18.2% in euploid embryos compared with 40% in segmental mosaic embryos. Furthermore, the LBR for euploid embryos was 53.8%, whereas for segmental mosaics, the LBR was 30%. The authors concluded that reporting segmental mosaicism was important to help with the selection of embryos for transfer and noted that although reduced, segmental mosaics still had the potential to result in a live birth.

Friedenthal et al. (2018) evaluated the difference in pregnancy outcomes using NGS compared with CGH for PGT-A in single frozen-thawed transferred embryos in a retrospective review. A total of 916 single frozen-thawed transferred embryo cycles from 2014 to 2016 were reviewed and included 548 NGS cases and 368 cases using CGH. The outcomes analyzed included implantation rate, LBR, and miscarriage rate. The NGS group had a higher implantation rate (72% vs 65%) than CGH and a higher LBR than CGH (62% vs 54%). The miscarriage rate was similar between the two groups. The authors concluded that NGS was better at detecting reduced-viability embryos caused by mosaicism and that using NGS may result in better pregnancy outcomes than CGH.

Barad et al. (2017) conducted a retrospective analysis of the impact of PGT-A on pregnancy outcomes in donor oocyte-recipient cycles. The authors used the data obtained between 2005 and 2013 from SART CORS. This database relies on voluntary reporting, and 90% of the U.S. IVF centers participate. In this cohort, first ETs with day 5 or 6 embryos were reviewed, for a total of 20,616 control cycles and 392 PGT-A cycles. The data showed that the pregnancy rates and LBRs were lower in the PGT-A group by 35% compared with the control group. The authors concluded that PGT-A was not associated with improved odds of pregnancy, live birth, or miscarriage rate.

Capalbo et al. (2015) compared SNP-based microarray screening, aCGH, and quantitative real-time PCR (qPCR) techniques for screening embryos. The authors conducted a prospective, double-blinded, observational study from October 2012 to December 2013. TE biopsies were done on day 5 to 6. Overall, 45 participants, who had indications of advanced maternal age or recurrent miscarriage or were a parental carrier of a balanced translocation, were included. A total of 124 blastocysts underwent aCGH. Of these, 122 survived warming and re-expansion and underwent TE biopsy and qPCR analysis. Two samples failed qPCR and were excluded. In total, 82% of embryos showed the same diagnosis between aCGH and qPCR, and 18% were discordant for at least one chromosome. Discordant blastocysts were warmed, and TE was biopsied again on 21 embryos that survived another rewarming and underwent a blinded SNP array analysis. A conclusive result was obtained in 18 of the 21. In four of these, the qPCR, aCGH, and SNP array did not match and were considered mosaic aneuploid. Overall, when the data were viewed per chromosome, the aCGH and qPCR results were consistent in 99.9% of cases in which both methods were performed on TE biopsy from the same embryo. However, the SNP-based reanalysis showed a higher discordant rate between aCGH and qPCR. The authors concluded that TE biopsies can be a highly reliable and effective approach for PGS and that until aCGH is studied for clinical negative predictive value, this comparative study can only demonstrate that aCGH results in a higher aneuploidy rate than other contemporary and better validated methods of chromosome screening.

Preimplantation Genetic Testing for Polygenic Disorders

PGT for polygenic disorders (PGT-P) is genetic testing that screens an embryo for disorders that involve multiple genes and provides a statistical prediction of increased clinical risk. Evidence for the utility of PGT-P for the selection of embryos is currently lacking, and ethical concerns exist related to the use of this technology.

In a recent systematic review of guidelines for PGT-M, Siermann et al. (2022) sought to (1) leverage PGT-M guidelines to better understand current issues and practice on the ethical acceptability of PGT-M and (2) make comparisons to PGT-P. Overall, 38 documents were reviewed, including national, European, and global guidelines. The researchers identified two main themes, including what PGT is considered appropriate for and who should make decisions regarding the use of PGT. They feel that many topics addressed in the PGT-M documents may apply to PGT-P as well; however, PGT-P screens for risks involving multiple polygenic conditions, which compounds the ethical challenges for this type of testing. There is a lack of regulatory guidance, guidelines, and/or position papers that address the ethical use of PGT-P. Ultimately, the authors concluded that based on the PGT-M documents reviewed, the ethical acceptability of PGT-P is limited at this time.

In a 2022 Precision Medicine Insight, Hayes addressed the use of PGT-P for the selection of embryos for implantation. The evidence was limited and focused mostly on models for validation of polygenic risk scoring that could be used for embryo screening. No studies that could inform the utility of PGT-P for embryo selection were identified. Per Hayes, professional guidelines that address the use of PGT-P for embryo selection were also limited and provided weak support against using PGT-P in this manner.

Clinical Practice Guidelines

American College of Medical Genetics and Genomics (ACMG)

In a 2024 Points to Consider Statement focused on the clinical utility of PGT-P for embryo selection, the ACMG states that further research is needed before PGT-P can be responsibly offered. In many clinical situations, the risks of PGT-P outweigh the benefits; this could lead to individual harm to either prospective parents, the future child, or both. More research on the social, ethical, and legal impact of PGT-P is warranted, and at this time, without proven clinical utility, PGT-P should be conducted only within research settings (Grebe et al., 2024).

The ACMG published, in 2023, a Points to Consider Statement that addresses the clinical application of polygenic risk scores (PRSs) (Abu-El-Haija et al.). This document states that the ACMG does not consider preimplantation PRSs appropriate for clinical use at this time, noting the potential legal, social, and ethical considerations related to PRSs in embryos.

In a 2021 position statement, the ACMG addresses direct-to-consumer prenatal testing for multigenic or polygenic disorders, indicating that issues surrounding testing for such disorders are very complex. These disorders have been shown to be controlled, at least in part, by multiple genetic loci and the potential influence of unknown environmental factors. The ACMG ultimately recommends that prenatal testing for diseases or disorders that exhibit polygenic or multigenic heritability is not appropriate for clinical use at this time and should not be offered direct to consumer.

American College of Obstetricians and Gynecologists (ACOG)

Committee Opinion Number 799 (ACOG, 2020; reaffirmed 2025) indicates that the clinical utility of PGT-M and PGT-SR is firmly established, but the utility of PGT-A has not yet been fully determined. ACOG further recommends the following:

- Confirmation of PGT-M results by chorionic villus sampling or amniocentesis should be offered to all patients.
- Confirmation of PGT-SR results by chorionic villus sampling or amniocentesis should be offered to all patients.
- Traditional diagnostic testing or screening for aneuploidy should be offered to all patients who have had PGT-A, in accordance with recommendations for all pregnant patients.

American Society for Reproductive Medicine (ASRM)

In a 2024 ethics committee opinion, the ASRM states that PGT-M for adult-onset conditions that are most commonly fully penetrant or confer disease predisposition is ethically justified. The following recommendations are made:

- Decisions regarding the use of PGT-M should be made by patients as they consider the risk of disease development, the role of disease severity, and the age at onset.
- An experienced PGT genetic counselor, with knowledge about both the condition and ART treatment, should play a significant role in the counseling of prospective patients who are considering using PGT-M for adult-onset conditions.
- Counseling from medical professionals with expertise in the condition is also appropriate.

A committee opinion intended to update and expand on the previous ASRM PGT opinion and provide specific information regarding PGT-M was published by the ASRM Practice Committee and Genetic Counseling Professional Group in 2023. The document asserts that the initial application of PGT-M was for prevention of severe, untreatable, or life-threatening diseases with onset in childhood; currently, this technology is being proposed for use across a wide range of genetic conditions for which there is more limited and/or controversial evidence. The 2023 opinion is summarized as follows:

- PGT-M should be offered if there is an identified significant reproductive risk.
- PGT-M is not recommended in cases of:
  - Autosomal recessive carrier status with no manifestation of symptoms.
  - A combination of variants that are not associated with disease.
  - Pseudodeficiency alleles.
  - Somatic-only variants.
- Comprehensive genetic counseling, including education regarding the condition in question and all reproductive options, is recommended for patients who are considering PGT-M.
- Counseling may also be beneficial after the results of PGT-M are obtained, particularly if ET decisions are being made.
- Considering technical limitations that have the potential to result in the misdiagnosis of an embryo, pregnancies that were conceived after the use of PGT-M should be offered prenatal testing to confirm embryo results and screen for other fetal anomalies.
- IVF clinics are encouraged to employ genetic counselors for workflow efficiency, smoother case management, and better experiences for patients who are considering PGT-M.

A revised committee opinion that addresses the clinical management of mosaic results from PGT-A was published by the ASRM Practice Committee in 2023. The updated opinion integrates additional studies focused on mosaic ET and offers up-to-date recommendations for the management of embryos with mosaic results from PGT-A based on the most current evidence. The document indicates that the value of PGT-A for universal screening in patients who are undergoing IVF has not been established, and, in fact, it has been shown to have no benefit for improvement of LBR in two RCTs (Yan et al., 2021; Munné et al., 2019). Still, the use of PGT-A is increasing in the United States; with this increase, the importance of suspected chromosomal mosaicism in embryos has become a topic of much discussion and controversy. The ASRM recommends comprehensive genetic counseling for all patients who are considering ET with PGT-A results that indicate mosaicism and for those who conceive after mosaic ET. The counselor should have specialty training in the realm of PGT and mosaic results. Referral to a pediatric geneticist is recommended for patients whose results indicate abnormal physical or developmental phenotypes.

In 2022, the ASRM Ethics Committee addressed the use of reproductive technology for the selection of sex for nonmedical reasons in an Ethics Committee Opinion. The opinion indicates that the use of PGT-A with IVF for sex selection only, with no medical indications, is ethically controversial and should not be encouraged. Discussion of knowledge of embryo sex at the time of transfer and the impact that this may have on embryo selection should take place at the time of informed consent for PGT-A, as PGT-A may be performed for indications unrelated to sex selection, with fetal sex as an incidental finding. The opinion asserts that providers who offer assisted reproduction services are not ethically obligated to either provide or refuse to provide methods of sex selection that are not medically indicated.

American Society for Reproductive Medicine (ASRM)/Society for Assisted Reproductive Technology (SART)

In a joint practice committee opinion (2024), the ASRM and SART state that while some studies have demonstrated higher birth rates after the use of PGT-A and SET, the studies have important limitations. They conclude that the value of PGT-A as a screening test for IVF patients has yet to be determined. Large, prospective studies that evaluate a variety of approaches to embryo selection are needed to determine the safety and risks of various technologies.

European Society of Human Reproduction and Embryology (ESHRE)

In 2023, ESHRE published good practice recommendations addressing add-ons in reproductive medicine. In this document, ESHRE states that the current evidence on PGT-A using contemporary genetic analysis methodologies shows limited improvement in LBRs. Assertions that PGT-A may reduce miscarriage rates or shorten time to pregnancy in specific patient groups, such as patients of advanced maternal age, are based primarily on post hoc analyses (e.g., Munné et al., 2019) and therefore require further high-quality, prospective research to establish their validity. Ultimately, ESHRE concludes that PGT-A is not recommended for routine clinical use.

A 2022 position statement from ESHRE supports the European Society of Human Genetics position regarding PRSs in PGT, acknowledging that PRSs can yield helpful data for populations by identifying at-risk groups but asserting that making predictions for patients is not reliable. In addition, ESHRE agrees with the European Society of Human Genetics

that significant ethical and scientific concerns exist around this technology. In summary, ESHRE states that the clinical utility of PRSs is low to absent for selection of embryos and does not support their use in clinical practice.

In 2020, ESHRE published a series of four papers that promote best practices in PGT; however, the authors note that the papers should not be interpreted as standard of care or inclusive/exclusive of other methods of care. ESHRE recommends that PGT should only be applied when the reliability of the diagnosis is high and potential contraindications (such as age; ability to retrieve gametes; or signs/symptoms of an autosomal dominant or x-linked disorder, which could cause medical complications during the IVF/pregnancy process) have been considered. Physical and psychological problems should be addressed as well. PGT testing is inappropriate in case of uncertain genetic diagnosis (for example genetic/molecular heterogeneity) or in case of an uncertain mode of inheritance. For identifying chromosome structural rearrangements, PGT-SR is a routine procedure in most IVF/PGT centers for patients who are unable to achieve a pregnancy or are at a high risk of pregnancy loss and/or abnormal live born births as a result of inheritance of unbalanced products of the rearrangement. However, PGT-SR is only recommended if the technique applied can detect all expected unbalanced forms of the chromosomal rearrangement. PGT-M testing is carried out to confirm pathogenic germline genetic variant(s) that may have serious health effects that could potentially manifest at birth, in childhood, or in adulthood. Exclusion or nondisclosure testing may be appropriate for late-onset disease, such as Huntington disease, to avoid presymptomatic testing of the patient with a family history of the disease. Exclusion testing is preferred over PGT, with nondisclosure of test results to the couple. Cited indications for PGT-A have included advanced maternal age, RIF, severe male factor, and recurrent miscarriage in couples with normal karyotypes; however, the value of PGT-A for all or a subset of patients undergoing IVF remains heavily debated and is the subject of ongoing discussions and research.

Preimplantation Genetic Diagnosis International Society (PGDIS)

The PGDIS updated their position statement regarding the transfer of mosaic embryos to include new evidence in 2021 (Leigh et al.). The position statement indicates that embryos with higher-level mosaicism appear to be associated with less favorable outcomes compared with lower-level mosaicism, and the relative percentage of mosaicism seems to better predict outcome than the involvement of specific chromosomes. As such, the relative percentage of mosaicism should be included in patient discussions and in reporting. The PGDIS further states that the decision to transfer a mosaic embryo can be prioritized, based either on the level or type of mosaicism, and if there is a choice between similar levels of mosaicism, preference may be considered based on morphology of the embryo or the nature of the variation. Comprehensive patient education and support regarding potential mosaic embryos and prioritization of euploid blastocysts continue to be part of the recommendations for clinicians.

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.

Laboratories that perform preimplantation genetic testing are regulated by the FDA under the Clinical Laboratory Improvement Amendments. Refer to the following website for more information: https://www.fda.gov/medical-devices/ivd-regulatory-assistance/clinical-laboratory-improvement-amendments-clia. (Accessed January 28, 2026)

A list of nucleic acid–based tests that have been cleared or approved by the FDA Center for Devices and Radiological Health is available at: https://www.fda.gov/medical-devices/in-vitro-diagnostics/nucleic-acid-based-tests. (Accessed January 28, 2026)

References

Abu-El-Haija A, Reddi HV, Wand H, et al.; ACMG Professional Practice and Guidelines Committee. The clinical application of polygenic risk scores: a Points to Consider Statement of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2023 May;25(5):100803.

ACMG Board of Directors. Direct-to-consumer prenatal testing for multigenic or polygenic disorders: a position statement of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2021 Nov;23(11):2027-2028.

Adamyan L, Pivazyan L, Obosyan L, et al. Preimplantation genetic testing for aneuploidy in patients of different age: a systematic review and meta-analysis. Obstet Gynecol Sci. 2024 Jul;67(4):356-379.

American College of Obstetricians and Gynecologists (ACOG). Preimplantation Genetic Testing. Committee Opinion Number 799. 2020 Mar;135(3):e133-137. Reaffirmed 2025. Available at: https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2020/03/preimplantation-genetic-testing. Accessed January 28, 2026.

Barad DH, Darmon SK, Kushnir VA, et al. Impact of preimplantation genetic screening on donor oocyte-recipient cycles in the United States. Am J Obstet Gynecol. 2017 Nov;217(5):576.e1-576.e8.

Beebeejaun Y, Bakalova D, Mania A, et al. Preimplantation genetic testing for aneuploidy versus morphological selection in women aged 35-42: results of a pilot randomized controlled trial. J Clin Med. 2025 Jul;14(14):5166.

Ben-Nagi J, Jones B, Naja R, et al. Live birth rate is associated with oocyte yield and number of biopsied and suitable blastocysts to transfer in preimplantation genetic testing (PGT) cycles for monogenic disorders and chromosomal structural rearrangements. Eur J Obstet Gynecol Reprod Biol X. 2019 Jun;4:100055.

Bhatt SJ, Marchetto NM, Roy J, et al. Pregnancy outcomes following in vitro fertilization frozen embryo transfer (IVF-FET) with or without preimplantation genetic testing for aneuploidy (PGT-A) in women with recurrent pregnancy loss (RPL): a SART-CORS study. Hum Reprod. 2021 Jul;36(8):2339-2344.

Bulletti FM, Sciorio R, Conforti A, et al. Causes of embryo implantation failure: a systematic review and metaanalysis of procedures to increase embryo implantation potential. Front Endocrinol. 2025 Feb;15:1429193.

Cai H, Kirshenbaum M, Zhang D, et al. Preimplantation genetic testing for aneuploidy on previously cryopreserved unbiopsied blastocysts: a cohort study in women with IVF pregnancy loss. Reprod Biol Endocrinol. 2025 Mar;23(1):31.

Capalbo A, de Wert G, Mertes H, et al. Screening embryos for polygenic disease risk: a review of epidemiological, clinical, and ethical considerations. Hum Reprod Update. 2024 Oct;30(5):529-557.

Capalbo A, Treff NR, Cimadomo D, et al. Comparison of array comparative genomic hybridization and quantitative real-time PCR-based aneuploidy screening of blastocyst biopsies. Eur J Hum Genet. 2015 Jul;23(7):901-906.

Chang J, Boulet SL, Jeng G, et al. Outcomes of in vitro fertilization with preimplantation genetic diagnosis: an analysis of the United States Assisted Reproductive Technology Surveillance Data, 2011–2012. Fertil Steril. 2016 Feb;105:394-400.

Cheng X, Zhang Y, Deng H, et al. Preimplantation genetic testing for aneuploidy with comprehensive chromosome screening in patients undergoing in vitro fertilization: a systematic review and meta-analysis. Obstet Gynecol. 2022 Nov;140(5):769-777.

Chow JFC, Yeung WSB, Lee VCY, et al. Evaluation of preimplantation genetic testing for chromosomal structural rearrangement by a commonly used next generation sequencing workflow. Eur J Obstet Gynecol Reprod Biol. 2018 May;224:66-73.

Department of Labor; Office of Disability Employment Policy; Federal Government Definition for Social Security Disability Benefits. Available at: https://www.dol.gov/odep/faqs/general.htm. Accessed January 28, 2026.

ESHRE Add-ons working group; Lundin K, Bentzen JG, Bozdag G, et al. Good practice recommendations on add-ons in reproductive medicine. Hum Reprod. 2023 Nov;38(11):2062-2104.

ESHRE PGT Consortium and SIG-Embryology Biopsy Working Group, Kokkali G, Coticchio G, Bronet F, et al. ESHRE PGT Consortium and SIG Embryology good practice recommendations for polar body and embryo biopsy for PGT. Hum Reprod Open. 2020 May;2020(3):hoaa020.

ESHRE PGT Consortium Steering Committee, Carvalho F (a), Coonen E, Goossens V, et al. ESHRE PGT Consortium good practice recommendations for the organisation of preimplantation genetic testing. Hum Reprod Open. 2020 May;2020(3):hoaa021.

ESHRE PGT-M Working Group, Carvalho F (b), Moutou C, Dimitriadou E, et al. ESHRE PGT Consortium good practice recommendations for the detection of monogenic disorders. Hum Reprod Open. 2020 May;2020(3):hoaa018.

ESHRE PGT-SR/PGT-A Working Group, Coonen E, Rubio C, Christopikou D, et al. ESHRE PGT Consortium good practice recommendations for the detection of structural and numerical chromosomal aberrations. Hum Reprod Open. 2020 May;2020(3):hoaa017.

Ethics Committee of the American Society for Reproductive Medicine. Use of preimplantation genetic testing for monogenic adult-onset conditions: an ethics committee opinion. Fertil Steril. 2024 Oct;122(4):607-611.

Ethics Committee of the American Society for Reproductive Medicine (ASRM). Use of reproductive technology for sex selection for nonmedical reasons: an ethics committee opinion. Fertil Steril. 2022 Apr;117(4):720-726.

European Society of Human Reproduction and Embryology (ESHRE). ESHRE supports the position of ESHG on embryo selection based on polygenic risk scores. February 2022. Available at: https://www.eshre.eu/Guidelines-and-Legal/Position-statements/PRS. Accessed January 28, 2026.

Friedenthal J, Maxwell SM, Munné S, et al. Next generation sequencing for preimplantation genetic screening improves pregnancy outcomes compared with array comparative genomic hybridization in single thawed euploid embryo transfer cycles. Fertil Steril. 2018 Apr;109(4):627-632.

Ginström Ernstad E, Hanson C, Wånggren K, et al. Preimplantation genetic testing and child health: a national register-based study. Hum Reprod. 2023 Apr;38(4):739-750.

Grebe TA, Khushf G, Greally JM, et al; ACMG Social, Ethical, and Legal Issues Committee. Clinical utility of polygenic risk scores for embryo selection: a Points to Consider Statement of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2024 Apr;26(4):101052.

Hayes, Inc. Precision Medicine Insights. Polygenic Risk Scores for Embryo Selection. Hayes, Inc.; April 21, 2022.

Hou W, Shi G, Ma Y, et al. Impact of preimplantation genetic testing on obstetric and neonatal outcomes: a systematic review and meta-analysis. Fertil Steril. 2021 Oct;116(4):990-1000.

Hu M, Liu M, Tian S, et al. Comparative analysis of pregnancy outcomes in preimplantation genetic testing for aneuploidy and conventional in vitro fertilization and embryo transfer: a stratified examination on the basis of the quantity of oocytes and blastocysts from a multicenter randomized controlled trial. Fertil Steril. 2024 Jul;122(1):121-130.

Huang C, Jiang W, Zhu Y, et al. Pregnancy outcomes of reciprocal translocation carriers with two or more unfavorable pregnancy histories: before and after preimplantation genetic testing. J Assist Reprod Genet. 2019a Nov;36(11):2325-2331.

Huang L, Bogale B, Tang Y, et al. Noninvasive preimplantation genetic testing for aneuploidy in spent medium may be more reliable than trophectoderm biopsy. Proc Natl Acad Sci U S A. 2019b Jul;116(28):14105-14112.

Iews M, Tan J, Taskin O, et al. Does preimplantation genetic diagnosis improve reproductive outcome in couples with recurrent pregnancy loss owing to structural chromosomal rearrangement? A systematic review. Reprod Biomed Online. 2018 Jun;36(6):677-685.

Iwasa T, Kuwahara A, Takeshita T, et al. Preimplantation genetic testing for aneuploidy and chromosomal structural rearrangement: a summary of a nationwide study by the Japan Society of Obstetrics and Gynecology. Reprod Med Biol. 2023 May;22(1):e12518.

Kakourou G, Kahraman S, Ekmekci GC, et al. The clinical utility of PGD with HLA matching: a collaborative multi-centre ESHRE study. Hum Reprod. 2018 Mar;33(3):520-530.

Konstantinidis M, Ravichandran K, Gunes Z, et al. Aneuploidy and recombination in the human preimplantation embryo. Copy number variation analysis and genome-wide polymorphism genotyping. Reprod Biomed Online. 2020 Apr; 40(4):479-493.

Kubikova N, Babariya D, Sarasa J, et al. Clinical application of a protocol based on universal next-generation sequencing for the diagnosis of beta-thalassaemia and sickle cell anaemia in preimplantation embryos. Reprod Biomed Online. 2018 Aug;37(2):136-144.

Kucherov A, Fazzari M, Lieman H, et al. PGT-A is associated with reduced cumulative live birth rate in first reported IVF stimulation cycles age ≤ 40: an analysis of 133,494 autologous cycles reported to SART CORS. J Assist Reprod Genet. 2023 Jan;40(1):137-149.

Leigh D, Cram DS, Rechitsky S, et al. PGDIS position statement on the transfer of mosaic embryos 2021. Reprod Biomed Online. 2022 Jul;45(1):19-25.

Li M, Kort J, Baker VL. Embryo biopsy and perinatal outcomes of singleton pregnancies: an analysis of 16,246 frozen embryo transfer cycles reported in the Society for Assisted Reproductive Technology Clinical Outcomes Reporting System. Am J Obstet Gynecol. 2021 May;224(5):500.e1-500.e18.

Liang Z, Wen Q, Li J, et al. A systematic review and meta-analysis: clinical outcomes of recurrent pregnancy failure resulting from preimplantation genetic testing for aneuploidy. Front Endocrinol (Lausanne). 2023 Oct;14:1178294.

Liu D, Chen C, Huang Q, et al. Preimplantation genetic testing for complex chromosomal rearrangements: clinical outcomes and potential risk factors. Front Genet. 2024 Jul;15:1401549.

Maithripala S, Durland U, Havelock J, et al. Prevalence and treatment choices for couples with recurrent pregnancy loss due to structural chromosomal anomalies. J Obstet Gynaecol Can. 2018 Jun;40(6):655-662.

Mao D, Xu J, Sun L. Impact of trophectoderm biopsy for preimplantation genetic testing on obstetric and neonatal outcomes: a meta-analysis. Am J Obstet Gynecol. 2024 Feb;230(2):199-212.e5.

Mei Y, Lin Y, Chen Y, et al. Preimplantation genetic testing for aneuploidy optimizes reproductive outcomes in recurrent reproductive failure: a systematic review. Front Med. 2024 Feb;11:1233962.

Mumusoglu S, Telek SB, Ata B. Preimplantation genetic testing for aneuploidy in unexplained recurrent pregnancy loss: a systematic review and meta-analysis. Fertil Steril. 2025 Jan;123(1):121-136.

Munné S, Kaplan B, Frattarelli JL, et al.; STAR Study Group. Preimplantation genetic testing for aneuploidy versus morphology as selection criteria for single frozen-thawed embryo transfer in good-prognosis patients: a multicenter randomized clinical trial. Fertil Steril. 2019 Dec;112(6):1071-1079.e7.

Nakano T, Ammae M, Satoh M, et al. Analysis of clinical outcomes and meiotic segregation modes following preimplantation genetic testing for structural rearrangements using aCGH/NGS in couples with balanced chromosome rearrangement. Reprod Med Biol. 2022 Jun;21(1):e12476.

Poulton A, Menezes M, Hardy T, et al. Clinical outcomes following preimplantation genetic testing for monogenic conditions: a systematic review of observational studies. Am J Obstet Gynecol. 2025 Feb;232(2):150-163.

Practice Committee and Genetic Counseling Professional Group of the American Society for Reproductive Medicine (ASRM). Indications and management of preimplantation genetic testing for monogenic conditions: a committee opinion. Fertil Steril. 2023 Jul;120(1):61-71.

Practice Committees of the American Society for Reproductive Medicine (ASRM) and the Genetic Counseling Professional Group. Clinical management of mosaic results from preimplantation genetic testing for aneuploidy of blastocysts: a committee opinion. Fertil Steril. 2023 Nov;120(5):973-982.

Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. The use of preimplantation genetic testing for aneuploidy: a committee opinion. Fertil Steril. 2024 Sep;122(3):421-434.

S, Zagers M, Kostova E, et al. Preimplantation genetic testing for aneuploidies (abnormal number of chromosomes) in in vitro fertilisation. Cochrane Database Syst Rev. 2020 Sep;9:CD005291.

Siermann M, Tšuiko O, Vermeesch JR, et al. A review of normative documents on preimplantation genetic testing: recommendations for PGT-P. Genet Med. 2022 Jun;24(6):1165-1175.

Simopoulou M, Sfakianoudis K, Maziotis E, et al. PGT-A: who and when? A systematic review and network meta-analysis of RCTs. J Assist Reprod Genet. 2021 Aug;38(8):1939-1957.

Taskin O, Hochberg A, Tan J, et al. Preimplantation genetic testing for aneuploidy in in vitro fertilization using comprehensive chromosome screening: a systematic review and meta-analysis. Int J Fertil Steril. 2024 Jun;18(3):185-194.

Tiegs AW, Tao X, Zhan Y, et al. A multicenter, prospective, blinded, nonselection study evaluating the predictive value of an aneuploid diagnosis using a targeted next-generation sequencing-based preimplantation genetic testing for aneuploidy assay and impact of biopsy. Fertil Steril. 2021 Mar;115(3):627-637.

Verpoest W, Staessen C, Bossuyt PM, et al. Preimplantation genetic testing for aneuploidy by microarray analysis of polar bodies in advanced maternal age: a randomized clinical trial. Hum Reprod. 2018 Sep;33(9):1767-1776.

Vlajkovic T, Grigore M, van Eekelen R, et al. Day 5 versus day 3 embryo biopsy for preimplantation genetic testing for monogenic/single gene defects. Cochrane Database Syst Rev. 2022 Nov;11(11):CD013233.

Volozonoka L, Perminov D, Korņejeva L, et al. Performance comparison of two whole genome amplification techniques in frame of multifactor preimplantation genetic testing. J Assist Reprod Genet. 2018 Aug;35(8):1457-1472.

Yan J, Qin Y, Zhao H, et al. Live birth with or without preimplantation genetic testing for aneuploidy. N Engl J Med. 2021 Nov;385(22):2047-2058.

Zegers-Hochschild F, Adamson GD, Dyer S, et al. The International Glossary on Infertility and Fertility Care, 2017. Fertil Steril. 2017 Sep;108(3):393-406.

Zheng W, Yang C, Yang S, et al. Obstetric and neonatal outcomes of pregnancies resulting from preimplantation genetic testing: a systematic review and meta-analysis. Hum Reprod Update. 2021 Oct;27(6):989-1012.

Zhou S, Cheng D, Ouyang Q, et al. Prevalence and authenticity of de-novo segmental aneuploidy (> 16 Mb) in human blastocysts as detected by next-generation sequencing. Reprod Biomed Online. 2018b Nov;37(5):511-520.

Zhou Z, Ma Y, Li Q, et al. Massively parallel sequencing on human cleavage-stage embryos to detect chromosomal abnormality. Eur J Med Genet. 2018a Jan;61(1):34-42.

Zore T, Kroener LL, Wang C, et al. Transfer of embryos with segmental mosaicism is associated with a significant reduction in live-birth rate. Fertil Steril. 2019 Jan;111(1):69-76.

Policy History/Revision Information

Date	Summary of Changes
05/01/2026	**Related Policies** • Added reference link to the Medical Policy titled *Whole Exome and Whole Genome Sequencing (Non-Oncology Conditions)* **Coverage Rationale** • Replaced language indicating "Preimplantation Genetic Testing (PGT) for monogenic/single gene defects (PGT-M) or inherited structural chromosome rearrangements (PGT-SR) is proven and medically necessary using polymerase chain reaction, next-generation sequencing (*e.g.*, chromosomal rearrangements), or chromosomal microarray for the [listed indications]" with "Preimplantation Genetic Testing (PGT) is proven and medically necessary *only* for monogenic/single-gene defects (PGT-M) or inherited structural chromosome rearrangements (PGT-SR) using polymerase chain reaction, next-generation sequencing (*i.e., for* chromosomal rearrangements), or chromosomal microarray for the [listed indications]" • Replaced reference to "gender" with "sex" **Supporting Information** • Updated *Description of Services*, *Clinical Evidence*, and *References* sections to reflect the most current information • Archived previous policy version CS160.M

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.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.