databases are dominated by Western European populations, although extending these databases to more diverse populations is a high priority of researchers and research funders, accompanied by a large recent effort to do so. Nevertheless, with few exceptions,[16] PRS still remain more predictive in populations with European ancestries. The "limited portability" of polygenic scores between populations highlights that their predictive value is derived only in part from genomic factors but also reflects environmental influences. This may have an even greater impact in the setting of embryo testing, where both the environment of the embryo and that of the future individual must be taken into account and may differ greatly from that of the reference genome database. These observations indicate that the clinical utility of PRS may be lower than expected because they have been based on GWAS of individuals of a narrow socioeconomic profile and fail to take the multiple facets of life history into account.

Points to consider

- The clinical utility of PRS may be affected by multiple factors: environmental interactions, phenotypic variability of the diseases, genetic admixture, and the presence of single-gene variants with large phenotypic impact. Screening for monogenic disorders should be offered and incorporated into PGT-P if clinical utility is achieved.
- Currently, disparities exist in PRS performance, limiting their portability. Although research is underway to close these gaps, data collection across many populations and socioeconomic groups should continue and be improved, and more generalizable methods should be implemented.
- ACMG has developed laboratory and clinical practice guidelines for PRS testing in adults that must be implemented before PRS testing can be integrated into other areas of clinical care.[8,9]

Application of PRSs for embryo selection

The application of PRS testing for embryo selection requires consideration of multiple factors in each step of the testing process. These include: (1) the impact of the IVF process itself on clinical utility of PGT-P, (2) the clinical validity of PGT-P, (3) ethical issues arising from different clinical scenarios in which PGT-P testing could be requested, and (4) challenges in providing informed consent and communicating disease risk information. We will discuss each of these, building the case for how they inform our consensus on whether PGT-P should be offered in clinical practice.

How does the IVF process affect risk/benefits of PGT-P?

In order to take advantage of PGT-P, interested persons must necessarily embark upon the lengthy and invasive process of IVF, which carries inherent risks of its own. These must be weighed against any potential benefit of the information gained through PGT-P. We consider those here, first providing background on the historical use of IVF, its benefits, and associated risks.

IVF has been utilized in clinical practice for over 40 years as a major method of assisted reproductive technology and has resulted in millions of live births, with consistent increases in both pregnancy and liveborn rates.[17] Although the most common reason to seek IVF is infertility, others include same-sex partner, single parent, risk for Mendelian disorder, risk of unbalanced chromosomal rearrangement, or personal/social concerns.

Multiple factors contribute to the success rate of achieving a viable pregnancy through IVF, including health factors of the pregnant person, intrauterine environment, laboratory techniques, and the genetic status of the embryo itself. The number of viable embryos that can potentially lead to a pregnancy varies widely, depending on the medical history of the parents, most significantly ovarian reserve.

Although the use of IVF has many benefits, there are risks associated with the process for the pregnant person and fetus. For individuals considering PGT-P, IVF and embryo biopsy are necessary procedures. In instances where IVF would not otherwise be utilized, potential harms to both the pregnant person and the fetus must be weighed against any potential benefit. Perinatal risks include preeclampsia, abnormal placentation, cesarean section, prematurity, low birth weight, and miscarriage. Studies of fetal risks of IVF have identified increased risks of birth defects, as well as imprinting disorders.

How does the process of PGT affect the risk/benefit of PGT-P?

PGT was first introduced in 1990 to test female embryos to prevent transmission of X-linked disorders (PGT-M) (American Society for Reproductive Medicine, ASRM). The introduction of next-generation sequencing has facilitated additional testing with greater accuracy to prioritize embryos for transfer. To overcome the negative effects of aneuploidy on pregnancy success rates and its impact on failed IVF and miscarriage, PGT for aneuploidy (PGT-A) was introduced, with the intent to improve implantation and live birth rates with IVF.[18,19]

A recent study noted that ongoing pregnancy rates and live birth rates are improved in those of advanced age ($\geq$ 38) with the implementation of PGT-A; however, because 32% of those studied did not have any viable embryos to transfer, the conclusion is not straightforward.[20] The clinical utility of PGT-A to select euploid embryos remains controversial because of lack of proof of efficacy in increasing live births.[21-26] Types of PGT currently utilized widely in clinical practice include PGT-A, PGT-M, and preimplantation testing for structural rearrangements (PGT-SR). Although PGT-A is widely utilized by reproductive endocrinologists, it has not been clinically validated nor is there strict oversight on its regulation.[27,28] The American College of Obstetricians and Gynecologists (ACOG) states that routine use of PGT-A for IVF in infertile women is not proven and