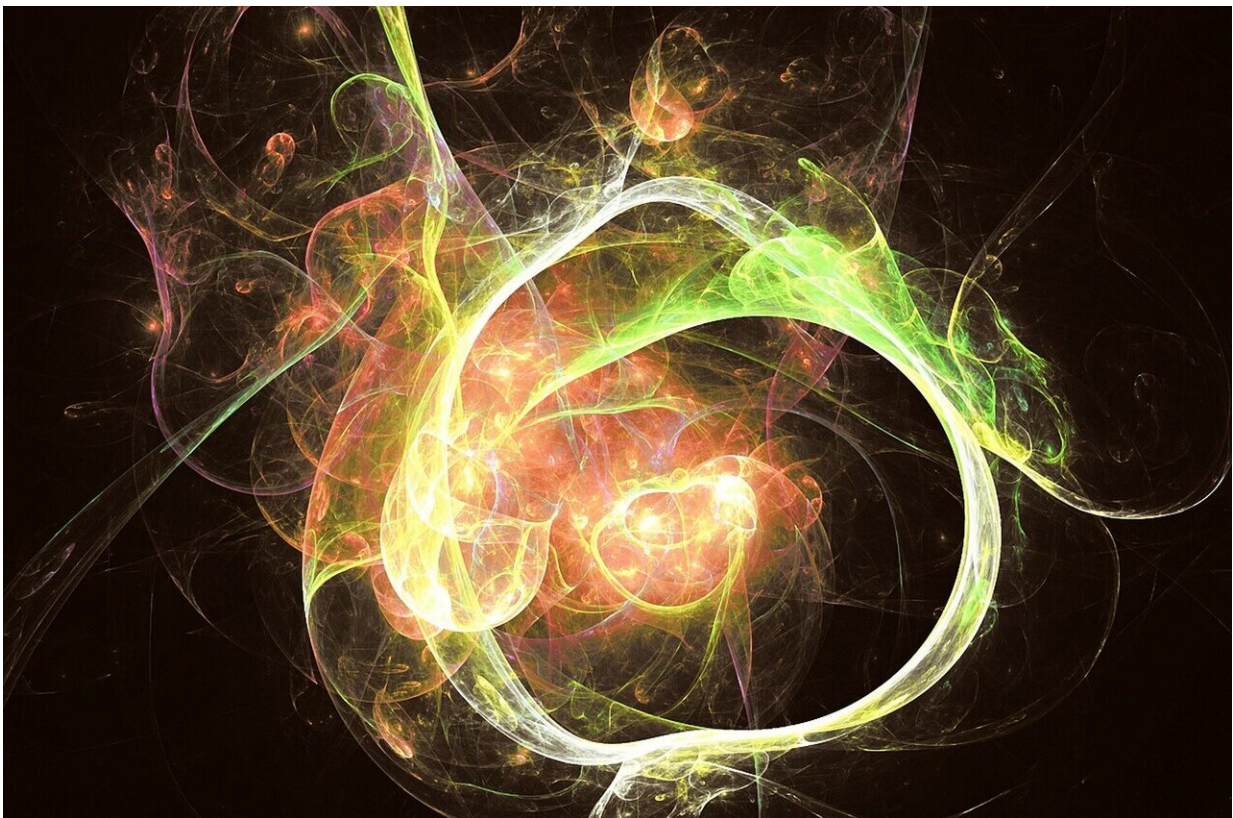


Report sounds alarm on efficacy, safety, ethics of embryo selection with polygenic scores

July 1 2021



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A special report published today in the *New England Journal of Medicine* raises serious questions about the benefits, risks and ethics of a new

service—which the authors call "embryo selection based on polygenic scores," or ESPS—that allows in vitro fertilization patients to select embryos with the goal of choosing healthier and even smarter children.

The multinational team of researchers describes the limitations of ESPS and warns of the risk that patients and even in vitro fertilization (IVF) clinicians may form the impression that ESPS is more effective and less risky than it is. The authors highlight that since the same gene often influences many different traits, ESPS designed to select for one trait can lead to the unintentional selection of adverse traits. They also warn about the potential of ESPS to alter population demographics, exacerbate socioeconomic inequalities and devalue certain traits.

If ESPS continues to be available to IVF patients, the researchers call on the Federal Trade Commission to develop and enforce standards for responsible communication about the service. The authors also call for a societywide conversation about the ethical use of the technology and whether it should be regulated.

Polygenic scores are predictions of individual health and other outcomes derived from genomewide association studies. Polygenic scores have been shown, in adults, to partially predict those outcomes. As the authors explain, however, their predictive power is significantly reduced when comparing embryos to one another.

"Polygenic scores are already only weak predictors for most individual adult outcomes, especially for social and behavioral traits, and there are several factors that lower their predictive power even more in the context of [embryo selection](#)," said Patrick Turley, assistant research professor of economics at the USC Dornsife College of Letters, Arts and Sciences and co-first author of the paper. "Polygenic scores are designed to work in a different setting than an IVF clinic. These weak predictors will perform even worse when used to select embryos."

Turley and colleagues modeled, for several diseases, the expected difference in the future individual's risk for the disease between using ESPS to select an embryo versus choosing an embryo at random among 10 viable embryos. In most cases, the absolute risk reduction from ESPS is very small. Moreover, these estimates are extremely uncertain, so much so that the effect of ESPS is swamped by background variation.

Multiple companies are now working with IVF clinics to offer ESPS to patients who want to select an embryo with a lower chance than other embryos of developing, as an adult, diabetes, cancer, heart disease, inflammatory bowel disease, Alzheimer's disease and schizophrenia. One company also offers ESPS for selecting embryos according to their predicted educational attainment, household income and cognitive ability. The founder of another company has not ruled out someday offering ESPS in some countries for skin color or above-average cognitive ability

(<https://www.genengnews.com/insights/polygenic-risk-scores-and-genomic-prediction-qa-with-stephen-hsu/>).

Drawbacks to ESPS

For ESPS to work, [polygenic scores](#) need to give at least moderately accurate predictions of whether the resulting individuals will have a certain trait or not. The genomewide association studies that generate the polygenic scores sometimes suggest moderate or even large differences in actual outcomes between people with high versus low polygenic scores, but those differences are based on a sample of people from different families. However, as Turley and colleagues note, ESPS usually involves comparing members of the same family, which significantly lowers the predictive power of polygenic scores.

Additionally, for statistical reasons, genomewide association studies are conducted with people with similar ancestries. Unfortunately, for a

variety of reasons, existing studies have disproportionately included people with European ancestries. As a result, most polygenic scores constructed today will be less predictive for people of other ancestries.

Finally, assessments of the predictive power of polygenic scores typically assume very similar environments for the generation that was enrolled in the original genomewide association study and the generation that will be born as a result of ESPS. But by the time an embryo selected by ESPS is an adult, they may face a very different environment, which will lower predictive power.

Even if the limited effectiveness of ESPS is accurately communicated to patients, widespread use of ESPS raises other risks. For instance, the researchers warn that use of ESPS could exacerbate existing health and other disparities, as ESPS is largely only accessible to the relatively wealthy and currently best predicts outcomes among those with European ancestries. ESPS might also amplify prejudice and discrimination by signaling that existing people with traits that parents select against are less valuable.

"Some countries have authorities that decide which traits [embryos](#) can be tested for," said Michelle N. Meyer, assistant professor of bioethics and a legal scholar at Geisinger Health System and co-first author of the special report. "But in the U.S., there is a strong legal and ethical tradition of viewing reproductive decisions as matters of private individual choice. In the short term, the FTC should help establish what counts as adequate evidence to support claims about the expected benefits of ESPS and what counts as adequate information disclosure in this context."

The researchers also call for professional medical societies to develop policies and guidance in this space and for companies themselves to demonstrate that the information they provide to diverse customers is

complete, accurate and well-understood.

They also say there needs to be a societywide conversation about whether using existing legal frameworks to ensure accurate information about ESPS is sufficient, along with if limits on the use of ESPS should be adopted.

"Many individual reproductive decisions, aggregated over generations, can have profound societal consequences," said Daniel J. Benjamin, corresponding author and a professor at the UCLA Anderson School of Management and David Geffen School of Medicine. "Collectively, these decisions could alter population demographics, exacerbate inequalities and devalue traits that are selected against."

Provided by University of Southern California

Citation: Report sounds alarm on efficacy, safety, ethics of embryo selection with polygenic scores (2021, July 1) retrieved 7 January 2024 from

<https://medicalxpress.com/news/2021-07-alarm-efficacy-safety-ethics-embryo.html>

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