Viewpoint: ‘Magic promised by genetically pruning ‘defective’ embryos has fairy-dusted the eyes of even the most intelligent’ — Maybe it’s time to hit the pause button

Advances in genetics have been revolutionized in the last few years. First came CRISPR, which can edit single genes, possibly preventing diseases with a single genetic determinant – raising the possibility of gene editing of children. CRISPR is too immature to be commercialized for this purpose, and this debate is speculative for now. But genome-wide association studies (GWAS) – which assesses the entire genome and can identify multiple genetic markers predictive of disease — have made landfall and are being commercialized for that purpose.

GWAS and polygenic risk scores (PGS)

Genome-Wide Associations Studies (GWAS) employ statistical means of describing the genome. They can be used to calculate polygenic risk scores or polygenic scores (they go by both names), which can tell you how your genetic constitution compares to others. It also can predict traits, including the risk of diseases caused by multiple genetic combinations. (Here’s more on GWAS and PGS).

But while your PGS can tell you that you may be at a higher *risk* of, say, coronary heart disease – it won’t tell you *when* you might get sick – or even *if* you will get sick at all. The most your PGS can tell you is your susceptibility to disease. Nor does PGS factor in contributory causes like environmental insults or lifestyle, diet, or stress, which also influence disease onset.

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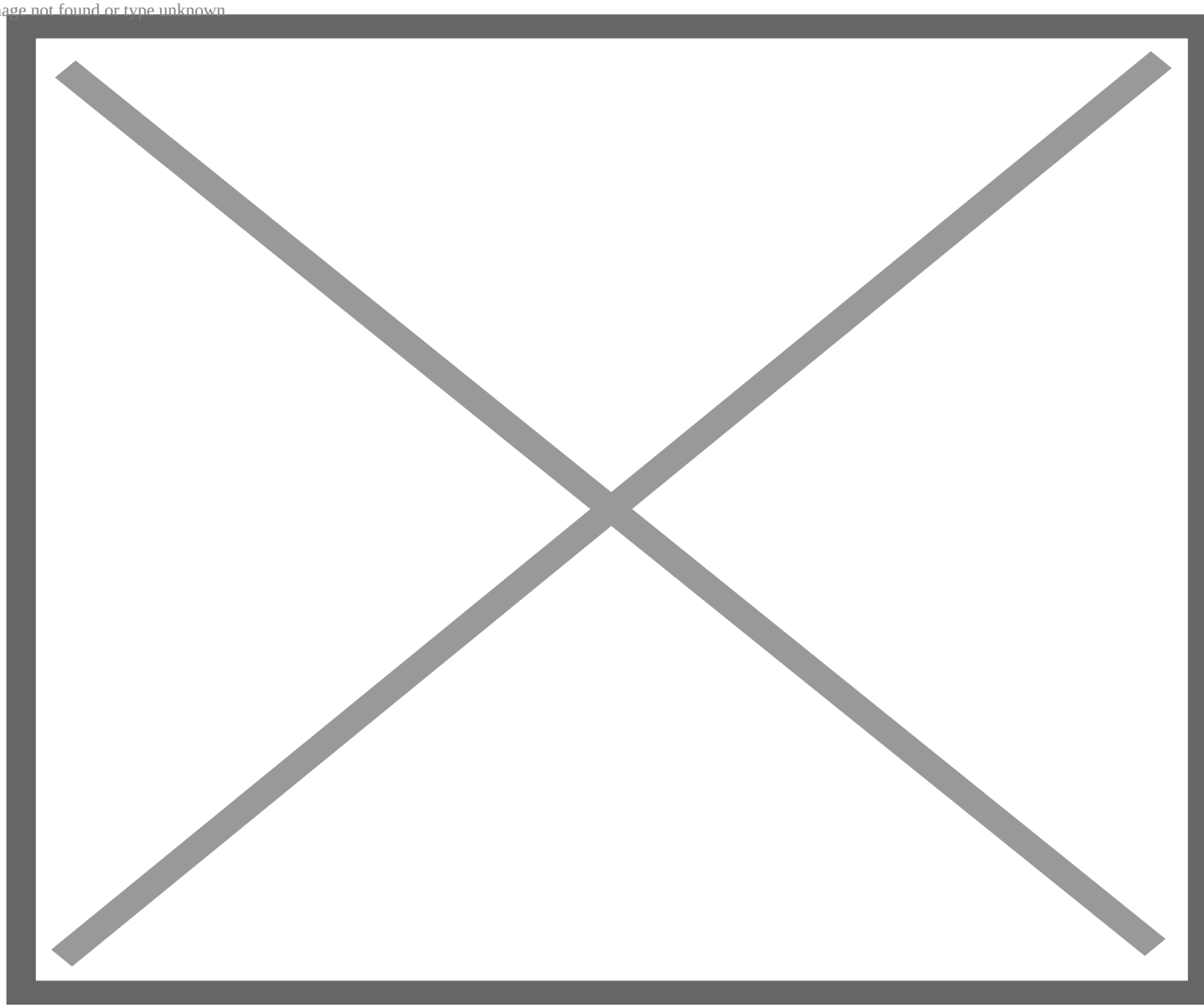


A diagram showing how a polygenic risk score could be interpreted. Credit: German Center for Cardiovascular Research

“Choice over chance”

PGS can tell you what’s bad about your genome – but it can also tell you what’s good about it. For reproductive entrepreneurs, this translated into using these scores to select the “best” embryo for implantation following In Vitro Fertilization (IVF). At least one American company advertises the technology to choose the healthiest embryo amongst the “litter” of recovered fertilized eggs.

It doesn't take much imagination to conjure the creation of a PGS for intelligence (some reports say it already exists and is available for the wealthy[1, 2]) or aesthetics, using an algorithm for height, body-mass index, eye and hair color, skin tone, facial symmetry and Fibonacci proportionality of features, or athleticism, including genetic markers for endurance, muscle mass, and strength. These scores would allow prospective parents to choose the embryo genetically destined to be the best looking, smartest, healthiest, or most athletic of their offspring – that is, if you don't place much importance on environmental and personality factors, such as drive, discipline, resilience, and motivation. (Although at least one evolutionary geneticist claims that even these factors are also genetically influenced [3])

Legally, in the United States, there is no problem using PGS to select the "best" embryo. Medically, it entails no additional risk to the embryo – IVF embryos are routinely screened for genetic markers that compromise gestation, anyway. So, the question remains: should this be done?

Human embryo. Credit: BioEdge

Bioethics and beneficence

At least two noted bioethicist-scholars advocate in favor of genetic selectivity of embryos- based on an idiosyncratic reading of beneficence (the obligation of an individual to act for the benefit of another), one of the four bioethical principles offered by Beauchamp and Childress.

Julien Savulescu claims it is a moral obligation for prospective parents to choose the "best" child, meaning the "most advantaged child, or at least the one with the greatest chance of having the "best life," under the theory of procreative beneficence. Considerations of the future implications of such use – amply depicted in fiction scenarios – are ignored. For Savulescu, the concept of *who* chooses what constitutes "best" is unimportant. As to whether "parents may be swayed by fashion, superstition, and outrageous conception of the good life," he (wrongly) claims there are legal constraints that aim to prevent the most egregious parenting choices.

Professor John Robertson holds a similar opinion invoking "procreative liberty," which allows using an IVF procedure even if it increased the child's risks of injury. To Robertson, "children born with these "afflictions" would not be "harmed" because the alternative future for them would be non-existence," [2] a belief that I do not share and have written at length.

The rights of the child (Autonomy)

Autonomy, another ethical principle proffered by Beauchamp and Childress, is the right of self-determination. Those disagreeing with using PGS to select "the best" embryo claim the child has a right to an "open future," and a parent who chooses the embryo scoring highest on one matrix might be directing the child in a direction adverse to what the child might have chosen herself.

Indeed, while parents typically chose a partner that facilitates a reproductive likelihood in a particular direction – good parents don't push their offspring down a particular path (lest they spend years and big bucks on a shrink's couch undoing this primordial programming). To allow parents to choose their child's precise genetic destiny from the moment of conception trespasses on the child's right to choose what life she or he would like.

Social justice – To treat everyone equally and equitably

The third Beauchamp and Childress principle is justice, encompassing social justice. Here, the potential for societal danger conjured by the technology seems to have been ignored entirely by proponents of using PGS for embryo selection. Until these technologies can be made available to everyone, they will be the province of the rich – whose children often begin life healthier by virtue of better environments, which is also said to boost intelligence scores (NB this is *not* to be confused with intelligence). With plastic surgery, they are prettier. With drugs, their athletic performance is enhanced. The disparities of health

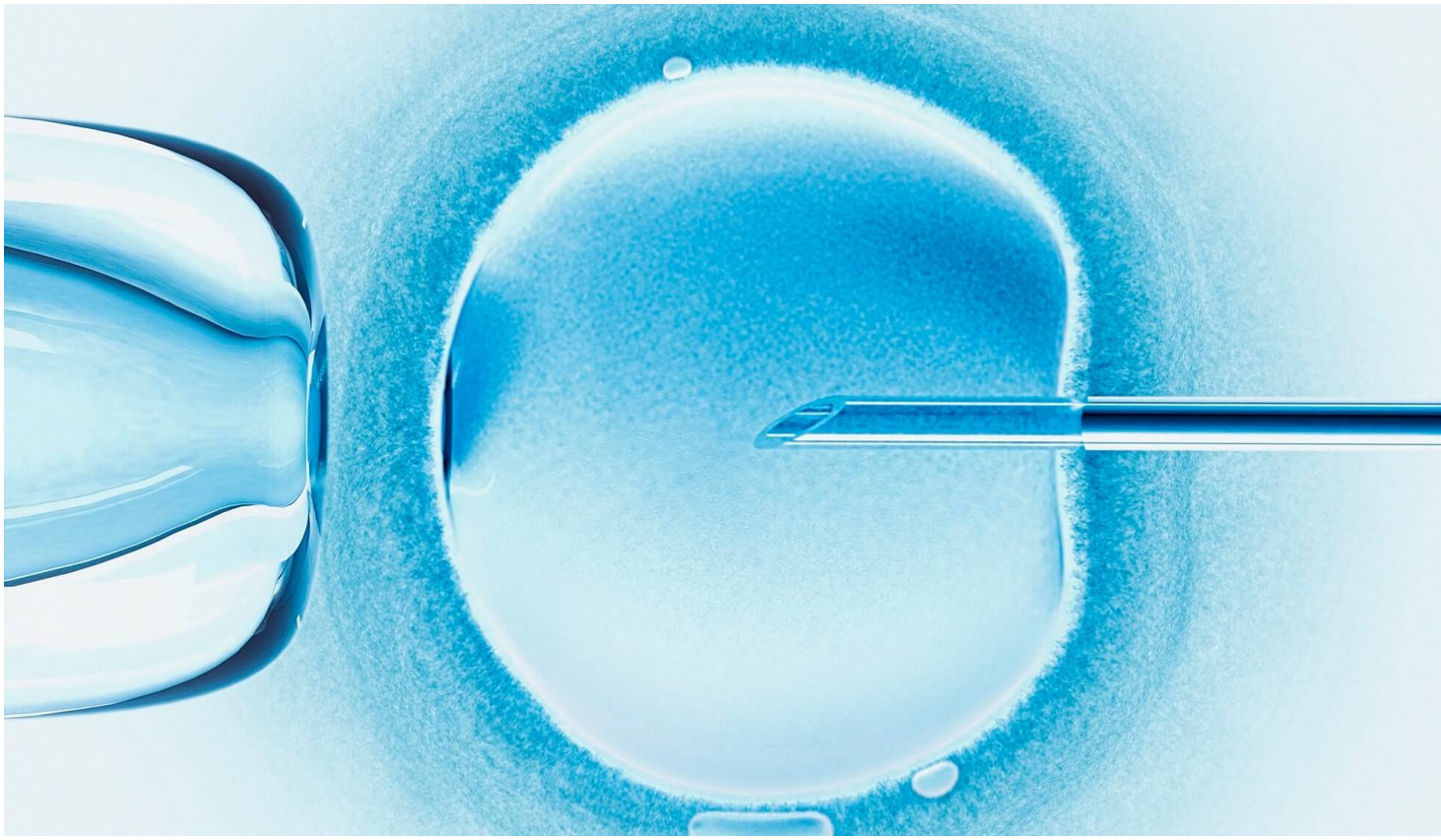
outcomes from socio-economic determinants are well-studied, and the availability of this technology to the rich, when not available to all – will only further expand the divide.

But even if the technology were available to all – let's say to enhance intelligence, it wouldn't make one child any smarter compared to the next– if she weren't already destined to be.

> If everyone might be genetically enhanced – *all* who are now smarter – would still be smarter genetically, their environments would still differ leading to the same state of affairs – at least relatively speaking [4]

Non-maleficence – IVF can be dangerous

The final Beauchamp and Children ethical principle is non-maleficence – do no harm. One might question using PGS at all, as it requires submitting to IVF. While IVF is a godsend to address infertility (and perhaps to select for children with certain immunological profiles to enable stem cell transplantation for sick siblings, as I've previously written), some suggest that IVF should not be routinely countenanced where infertility is not an issue – as the procedure entails rare risks of its own both to mother and child-to-be, being responsible for a slight increase in birth defects among other problems(4).



Depiction of in-vitro fertilization (IVF). Credit: Allure

Truth in advertising and biological validity

Most of those in the know recognize that PGS are predictive only for populations.

> We can certainly use genetics to look at statistical effects across populations, but this will give at best very fuzzy predictors for individuals.
>
> – Dr. Kevin Mitchell, geneticist [1]

Perhaps when there is only one “prize” being contested for, say, health, it might make sense to allow parents to choose the embryo with the probability of being “healthiest” (defined according to today’s technology). But when we include the choice between various packages – all involving probability functions – no definite outcome can be predicted. How could one reasonably choose between an embryo with a 90% chance of being healthy or one with a 60% chance of being more intelligent than her siblings?

Perhaps more egregious is the failure to recognize the impact of pleiotropism, meaning that one gene has multiple effects. This consideration is important both in CRISPR gene-editing and PGS determinations.

Pleiotropisms come in two varieties, vertical and horizontal. In the first, the genetic variant under question affects one trait, say cholesterol, which in turn affects others, like the risk of heart disease. Of more concern are the horizontal variants, where one gene has multiple non-related effects. So, say you want to create a child with the least risk of mental health issues – including a minimal risk of schizophrenia. Genes associated with reduced schizophrenia risk are also associated with both low and high body mass – meaning if you choose "against" schizophrenia, you might also be selecting "for" a child likely to be obese. Since we aren't conversant yet with the extent of genetic pleiotropisms, the unanticipated consequences of using PGS strongly cautions against its use at present.

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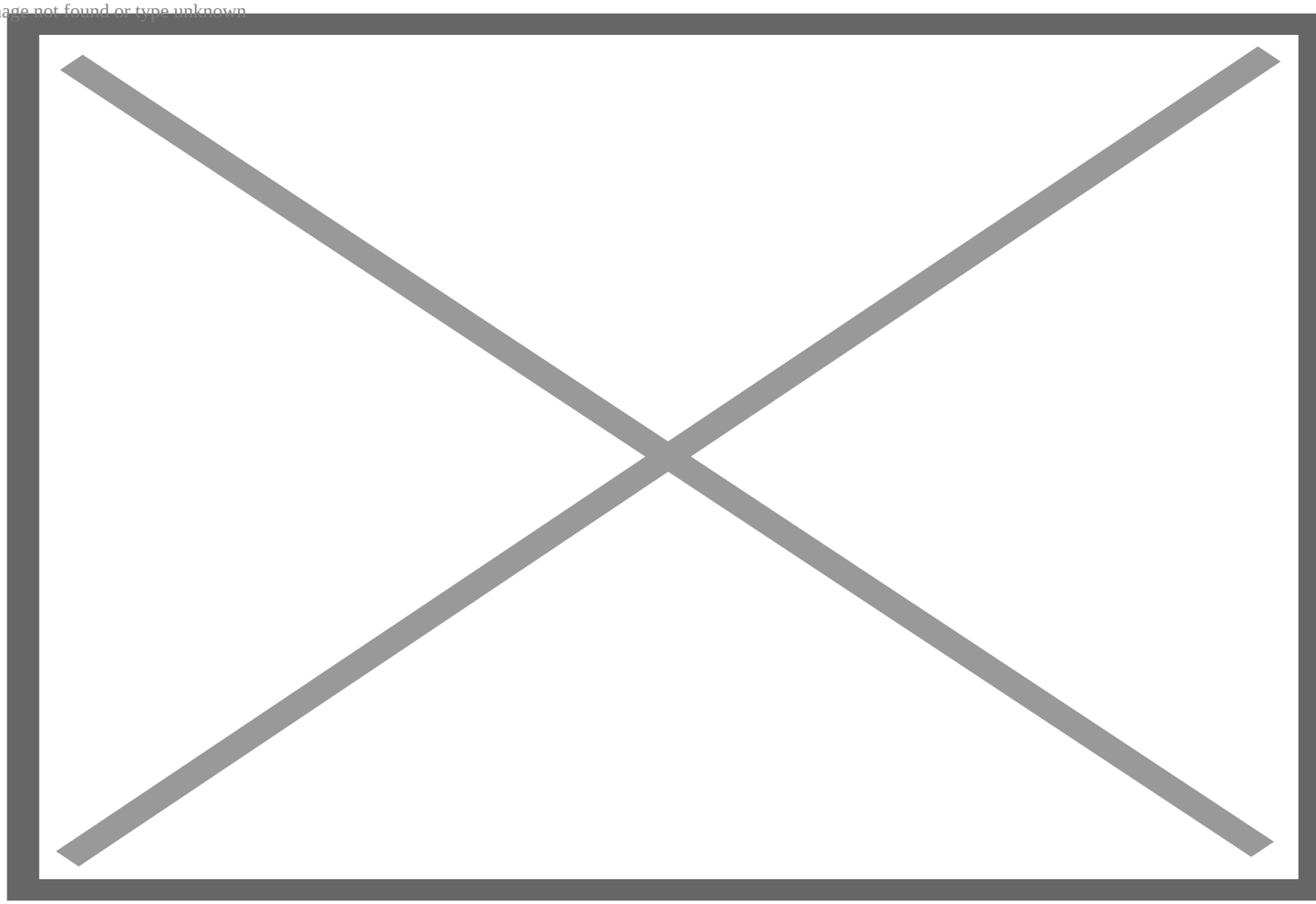

Credit: Boston Globe

Morality and humanity

The magic promised by these technologies seems to have fairy-dusted the eyes of even the most intelligent. This raises the phantasm of PGS or gene-editing to cure or eliminate diseases, like schizophrenia, Lou Gehrig's disease, dyslexia, or dwarfism. How wonderful, we think, to eliminate these

diseases from the face of the Earth. Perhaps not.

Had we given the parents of embryos containing markers for these diseases the chance to avoid birthing children with them, society would have been deprived of the contributions of John Nash (the Nobel prize winner in Mathematics), theoretical physicist Stephen Hawking, Carol Greider, the Nobel Laureate who discovered telomerase, and Professor Charles Steinmetz, the electrical engineering genius who boosted our capacities in electrical power systems, just to name a few who suffered from these conditions. And people who don't achieve high scores on any PGS rubric, like my friend's dear daughter, would be denied existence if these scores were in common use – prevented from enriching and brightening our lives with their smiles, kindness, and their good cheer.

Notes:

[1] Hannah Crichtlow, The Science of Fate, Hodder Press [2] O. Carter Snead, What It Means to be Human, Harvard University Press [3] Robert Plomin, Blue Print How DNA Makes Us Who We Are MIT Press (2018) [4] *Genetically-Engineered Begots, Have-Nots, and Tinkered Tots: (High Scoring PolyGenic Kids as a Heredity-Camelot) – An Introduction to the Legalities and Bio-Ethics of Advanced IVF and Genetic Editing* *SSRN.com* 3851431, Chicago-Kent Law Review (forthcoming) 2021

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