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Public views on polygenic screening of embryos:

Understanding moral acceptability and willingness to use is crucial for informing policy

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For decades, people have used genetic information to exercise control over the kinds of children they will have. These technologies have largely targeted chromosomal and monogenic disorders and traits; but most human phenotypes are highly polygenic (and influenced by the environment). One technology that targets the entire genome—preimplantation genetic testing for polygenic risk (PGT-P)—uses polygenic indexes (PGIs) to predict the expected value of the phenotype(s) that would arise for each embryo if successfully transferred; parents can use these predictions to select an embryo for in vitro fertilization (IVF). Seeing gaps in evidence and analysis relevant for potential policy discussions around PGT-P, we conducted a survey of public attitudes. Our data suggest that it would be unwise to assume that use of PGT-P—even for controversial traits—will be limited to idiosyncratic individuals, or that it has little potential to cause or contribute to society-wide changes and inequities.

Historically, technologies to enable control over offspring have included carrier screening, ultrasound, preimplantation genetic diagnosis, amniocentesis, chorionic villus sampling, noninvasive prenatal screening, and selective abortion. Using them, people have selected against diseases such as Huntington's, Down syndrome and other trisomies, and alleles

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SUPPLEMENTARY MATERIALS

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[such as pathogenic breast cancer gene (*BRCA*) variants] that increase an individual's lifetime risk of certain diseases. They have also selected for biological sex and conditions such as deafness. In contrast to those, a PGI—also called a polygenic risk score—is based on the estimated associations (calculated from a large-scale genetic study) between common genetic variants and a particular phenotype. This gene-based index can then be used to make phenotypic predictions—not only to avoid serious disease but also to try to select for phenotypes such as greater cognitive ability or educational attainment.

Another technology that targets the entire genome and could, in principle, vastly expand our ability to select for or against any heritable phenotype is germline genome editing (hereafter "gene editing")—for instance, with clustered regularly interspaced short palindromic repeats (CRISPR). This might someday be used to try to influence offspring characteristics by making thousands of DNA edits (or more) to a gamete or embryo.

However—with the notable exception of three Chinese children whose C-C chemokine receptor type 5 (*CCR5*) genes were illicitly edited while they were embryos in a misguided attempt to provide them with AIDS resistance (1, 2)—gene editing has not been used. Indeed, it is not permitted in some 70 countries (1), and experts have called for a global moratorium (2).

PGT-P, by contrast, is already offered by at least one US company whose embryo screening business operates in several countries and US states (3). Yet it has received far less academic, policy, and regulatory analysis than gene editing, leading to calls for urgent research about public attitudes towards PGT-P (4). Recent surveys have measured acceptance of gene editing (5, 6), intentions to use gene editing (7), and views about whether certain forms of embryo selection should be legally permitted (8). Someone's view about whether the law should prohibit a technology may be distinct from their view of whether the technology is morally acceptable, and both may be distinct from whether they themselves would use the technology. To our knowledge, this paper is the first to measure PGT-P use intentions—and the effects of social norming on these intentions.

ACCEPTABILITY AND WILLINGNESS

In January 2022, we conducted a preregistered, nationally representative US survey-based experiment on the attitudes of 6823 people towards three services: PGT-P, gene editing, and—as a nongenetic benchmark for attitudes toward interventions targeted at college admissions—courses to prepare for the SAT test (effective N after applying weights, 3805; see table S1 for sample characteristics). We randomized participants to answer two questions, in randomized order, about one of these three services. One question asked whether the respondent views the service as morally acceptable, morally wrong, or not a moral issue; participants could also indicate whether they were unsure. For this question, both PGT-P and gene editing were described as being potentially used for "medical and nonmedical traits."

The other question measured willingness to use each service by asking participants how likely it was—on a scale from 0 to 100%—that they would use the service to increase the

odds that their offspring will attend a top-100 college by selecting for genetic variants, or enrolling their child in courses, associated with higher educational attainment. We asked participants to assume that each service was free. We also asked them to assume a realistic effect size: We told them that about 3% of high school seniors attend a top-100 ranked college, and that each service would raise their likelihood of having such a child by two percentage points (from 3 to 5%). In the cases of gene editing and PGT-P, we asked them to assume that they were already using IVF and that the add-on service was safe. Finally, we further randomized participants within each "service condition" to be told that it was used on average by either "1 out of every 10" or "9 out of every 10" similarly situated people (for the PGT-P and gene editing arms, "people currently having babies"; for the SAT prep arm, "people who currently have high-school–age children").

SOCIAL NORM, AGE, AND EDUCATION

A minority of participants (41%) said they had no moral objection to gene editing for "certain medical and nonmedical traits" (i.e., they reported it was morally acceptable or not a moral issue), and a majority of participants reported no moral objection to PGT-P (58%) or SAT prep (76%) (fig. S1 and table S2). On average, participants said they were 34% likely to use gene editing, 43% likely to use PGT-P, and 69% likely to use SAT prep to increase the odds of their child attending a top-100 college (see the figure and table S2). Furthermore, a material fraction of participants reported a >50% likelihood of using each service (28% gene editing, 38% PGT-P, 68% SAT prep; table S2). As predicted, those who were told that 90% of relevant people use each service were more likely to say that they, too, would use it, compared to those who were told that 10% of people were using it. The mean willingness to use gene editing, PGT-P, and SAT prep was 4 ($P = 0.020$), 5 ($P = 0.007$), and 4 ($P = 0.022$) percentage points higher, respectively, for those in the 90% condition (table S3). These effect sizes are typical of those reported for behavioral intentions from other social norm manipulations.

A recent study of 2233 UK residents between the ages of 16 and 75 found that those under 35 were more likely than older participants to "support" (rather than "oppose") both sex selection by IVF patients and embryo gene editing for "preferred characteristics" such as "eye color, height, hair color, etc." (5). In the first of two exploratory analyses that we conducted, although the moral attitudes of those under 35 years of age toward all three services were statistically indistinguishable when compared to the full sample (all P values > 0.59; fig. S1 and table S4), those under 35 reported a higher willingness than the full sample to use gene editing (41% versus 34%, $P = 4.0 \times 10^{-4}$), PGT-P (48% versus 43%, $P = 0.013$), and SAT prep (72% versus 69%, $P = 0.039$) for educational attainment (see the figure and table S4). (All of these estimates account for sample overlap between the two groups; the statistically equivalent tests comparing those under 35 and those 35 and older are in table S4.) Approximately equal moral acceptance among age groups but differential willingness to use these services might reflect younger people being the natural use population for reproductive technologies and (as recent students rather than parents) SAT prep.

In the second exploratory analysis, compared to those with less educational attainment, those who had at least a bachelor's degree were more likely to say that gene editing (46% versus

39%, $P = 0.012$), PGT-P (65% versus 54%, $P = 1.7 \times 10^{-4}$), and SAT prep (86% versus 71%, $P = 3.9 \times 10^{-10}$) are morally acceptable or not a moral issue (see the figure and table S5). They also reported a greater likelihood that they themselves would use gene editing (38% versus 32%, $P = 0.008$), PGT-P (48% versus 40%, $P = 1.6 \times 10^{-4}$), and SAT prep (78% versus 67%, $P = 4.7 \times 10^{-17}$) to increase the odds that their child attends a top-100 college (see the figure and table S5). These results might reflect parents' tendency to try to mirror their own educational outcomes in the outcomes of their offspring, which would have implications for other phenotypes.

DISCUSSION

In the US, there appears to be both greater moral acceptance of, and greater willingness under certain circumstances to use, PGT-P versus gene editing—and the more people use PGT-P, the more likely others say they would, too. Those circumstances, of course, matter. We asked participants to assume that each service is safe; because CRISPR currently carries considerable risks to offspring (2), our results may overestimate acceptability of and willingness to use CRISPR. Additionally, we (accurately) portrayed PGT-P as available but gene editing as a future technology; people's views of gene editing might become more positive if it becomes available. To isolate participants' attitudes about shaping offspring characteristics, in assessing willingness to use, we also asked them to assume that each service was free—and, for PGT-P and gene editing, that they were already using IVF. Our data thus do not measure willingness to use PGT-P or gene editing among those who would not otherwise already be using IVF. However, the number of babies born through assisted reproductive technologies has more than tripled between 1996 and 2017 (9). Moreover, developments in stem cell research are expected to make IVF much less financially and physically costly (10).

Other aspects of the scenario we presented suggest that our results may represent an underestimate of acceptability and potential uptake. For one, in measuring potential uptake, we asked about an especially controversial use of these technologies: not to avoid serious disease, but to increase the odds that the resulting child will be admitted to a top-100 college. Prior surveys measured attitudes toward gene editing and PGT-P without quantifying how effective the technology would be, whereas we stipulated a realistic effect size (see supplementary materials). In prior research, we expressed concern that an unrealistic lay view of what PGT-P can deliver might drive appetite for the service. We recommended (inter alia) that advertised effect sizes focus on absolute gains rather than relative (proportional) gains, which seem large in part because they are calculated from a small base (11). Others have similarly warned that PGT-P is of "limited utility" for phenotypes such as height and cognitive ability (12). Yet, although we cannot know whether the realistic effect size that we stipulated, appropriately communicated in absolute terms, was perceived by participants as large or small, it still resulted in a substantial share of people expressing interest in using PGT-P.

As important as how many people are interested in PGT-P is which people are interested. That potential uptake is higher among younger generations compared to the full sample is notable, because younger generations are the ones who are in a position to use PGT-P.

Some critics of PGT-P argue that the technology's effectiveness in selecting for offspring phenotype is trivial. But PGT-P has been estimated by multiple independent researchers to have some impact, even if the expected gains are not what some consumers might imagine and some companies might suggest (11-13). That those who themselves have higher educational attainment are more interested in using PGT-P for this phenotype raises the risk that PGT-P will exacerbate existing inequalities. Over several generations, the gains from PGT-P could build on one another, resulting in familial transfers of socially-favored phenotypes that mirror and—given the costs of IVF—amplify unequal familial transfers of wealth.

CONCLUSION

Media reports of early adopters of PGT-P might suggest that it is a fringe issue unworthy of policy attention (14). But the sharp turn in public opinion about IVF itself shows that innovations that are initially met with limited uptake and even active resistance can quickly become normalized and widely adopted. A 1969 Harris poll found that most Americans objected to IVF, and the American Medical Association called for a moratorium on IVF research. In 1978, 1 month after the well-publicized birth of the first IVF baby, the same poll found that over 60% supported IVF and would consider using it themselves (15). In our survey, 78% said they view IVF as morally acceptable or not a moral issue; only 6% said it was morally wrong (table S6). A 2016 survey of 185 countries, including the US, found that only 18% "agreed with the use of" gene editing for intelligence, and a 2017 survey of 11 countries, again including the US, found very little intention to use gene editing to "enhance" offspring "memory and learning capacities" and little variation across countries (7). In light of our recent findings of much higher gene editing acceptance (41%) and substantial gene editing and PGT-P use intentions in the US to increase educational attainment, it is plausible that considerable gene editing and PGT-P use intention now also characterizes attitudes in other countries.

Public views of technology should influence policy-making in a democratic society. Experts who are critical of a technology should not assume that the public shares their knowledge or viewpoint. Understanding which members of the public are most likely to use a technology can inform predictions about societal impact—for example, the extent to which it is likely to enlarge existing or create new disparities. Much more should be learned about the public's reflexive as well as considered judgments. For instance, which other traits do people want to select for or against? How does relaxing the assumptions of free access and safety affect the rates, and distribution across groups, of moral acceptability and willingness to use? We should learn the extent to which people who would not otherwise use IVF would do so to use PGT-P. More subtly, legal frameworks for reproductive technologies vary widely (1); the current US path is one of continuing to treat offspring-influencing technologies as a matter of individual, private choice, despite their potential societal impact. People might have preferences against societal inequality that coexist with the preference to improve outcomes for their own family members. Specifically, someone might prefer that inequality be reduced at the aggregate level, but still choose an inequality-amplifying technology for themselves. Our study does not explore these issues, and future work should.

But despite their relevance, public attitudes alone do not determine appropriate policy. Additional research and diverse expert input should inform several policy questions: Given our limited knowledge of the unintended effects of selecting for and against particular phenotypes, does widespread use of PGT-P pose acceptable population risks? How can the complexities of PGT-P—e.g., pleiotropy, relative risk reduction—be conveyed to achieve appropriate consumer literacy? Given the costs of PGT-P and those of IVF and that PGIs developed with participants of European genetic ancestries are less predictive for those of other genetic ancestries, we must consider the extent to which a free market for PGT-P might exacerbate or create new health or social inequities, and ask whether society should tolerate that result. How can we ensure that those with traits that others select against remain fully welcomed members of our society? Should PGT-P be limited to certain traits, and if so, who would draw that line, and how? Finally, in the wake of the 2022 decision by the US Supreme Court in *Dobbs v. Jackson Women's Health Organization*, the US is experiencing uncertainty about the legal status not only of abortion but also of other reproductive decisions that are unprecedented in the past half century. Could choices about PGT-P be regulated without further threatening other reproductive choices?

Aside from urging the Federal Trade Commission to ensure proper communication of PGT-P and its expected gains (10), we do not prejudge what additional regulation, if any, is warranted. But we call on any policy choice—including not to further intervene—to be made deliberately, after input by experts and the public.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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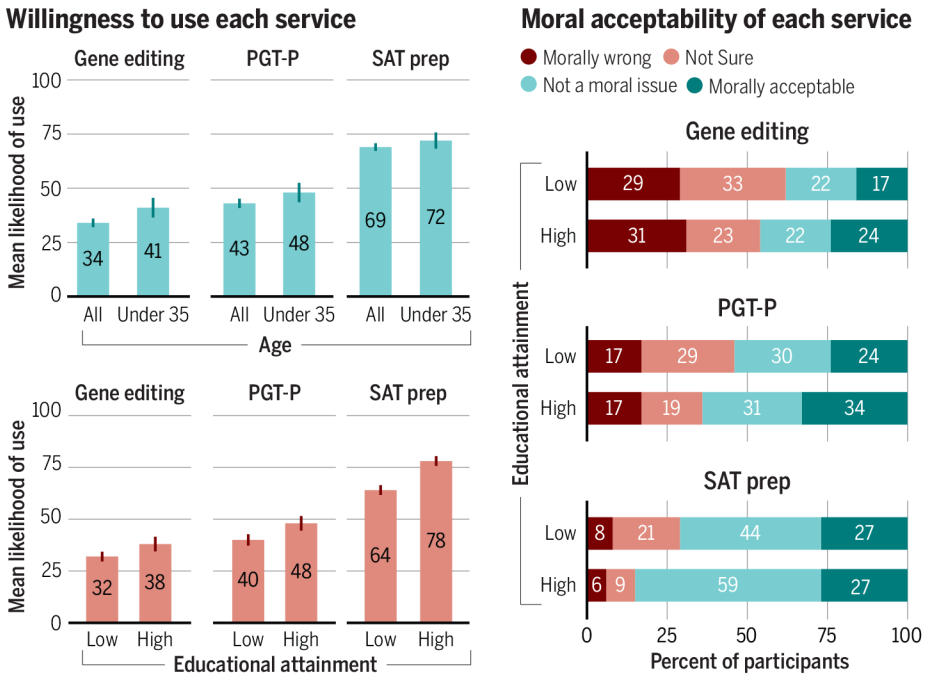
REFERENCES AND NOTES

1. Baylis F, Darnovsky M, Hasson K, Krahn TM, CRISPR J. 3, 365 (2020). [PubMed: 33095042]
2. Lander ES et al., Nature 567, 165 (2019). [PubMed: 30867611]
3. LifeView, https://www.lifeview.com/tests_pgtp.html.
4. Lázaro-Muñoz G, Pereira S, Carmi S, Lencz T, Genet. Med 23, 432 (2021). [PubMed: 33106616]
5. Progress Educational Trust, "Fertility, Genomics and Embryo Research: Public Attitudes and Understanding," June 2022; https://www.progress.org.uk/wp-content/uploads/2022/06/pet_fertilitygenomicsembryoresearch.pdf.
6. McCaughey T et al., Cell Stem Cell 18, 569 (2016). [PubMed: 27152441]
7. Gaskell G et al., Nat. Biotechnol 35, 1021 (2017). [PubMed: 29121022]
8. Zhang S, Johnson RA, Novembre J, Freeland E, Conley D, Soc. Sci. Med 274, 113796 (2021). [PubMed: 33684700]
9. Sunderam S et al., MMWR Surveill. Summ 69, 1 (2020).
10. Greely HT, The End of Sex and the Future of Human Reproduction (Harvard Univ. Press, 2018).
11. Turley P et al., N. Engl. J. Med 385, 78 (2021). [PubMed: 34192436]

12. Karavani E et al., Cell 179, 1424 (2019). [PubMed: 31761530]
13. Lencz T et al., eLife 10, e64716 (2021). [PubMed: 34635206]
14. Goldberg C, "The Pandora's box of embryo testing is officially open," Bloomberg, 26 May 2022; https://www.bloomberg.com/news/features/2022-05-26/dna-testing-for-embryos-promises-to-predict-genetic-diseases#xj4y7vzkg.
15. Bell AV, in Misconception: Social Class and Infertility in America (Rutgers Univ. Press, 2014), p. 6.



Moral acceptability and willingness to use, by age and education

Left: Mean likelihood of using gene editing, preimplantation genetic testing for polygenic risk (PGT-P), and courses to prepare for the SAT college admissions test, to increase participants' chances of having a child who attends a top-100 college by 2 percentage points (from 3% to 5%). Error bars are 95% confidence intervals. Low educational attainment reflects associate degree or below, high reflects bachelor's degree or above. See supplementary materials for *P* values and standard errors. Right: Degree of moral acceptability of each service. Some bars do not sum to 100% owing to rounding.