Potential perils of germline genomic engineering

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Introduction

Human germline genomic engineering would enable parents to choose to endow their children with any of a wide variety of traits: from exceptional health, lifespan, wellbeing, and cognitive capacity; to, potentially, personality traits, political leanings, and social dispositions. The enormity of the potential benefits is self-evident, and begs for speedy development of the technology.

Because germline engineering (GE for short) will have such strong and wide-ranging effects, it also comes with many perils—many possible bad outcomes in various spheres of life. In order to decide wisely about the development and application of GE technology, this article describes possible bad outcomes caused by GE.

The rest of this Introduction section describes in more detail the aim and structure of this article; the following sections, starting with "Unnaturalness", list perils of GE.

Germline engineering

Human germline genomic engineering creates human children with genomes that have been vectored in some way. The two broad types of genomic vectoring are multiplex genetic editing and genomic selection. Genetic editing targets several genetic loci and modifies the DNA at those loci, generally via some CRISPR-Cas9 system, either swapping, adding, or deleting one or more base pairs. Genomic selection assembles a haploid or diploid genome from subsegments of one or more genomes by some process other than natural gametogenesis and fertilization, where segments that score highly on a polygenic score (PGS) are favored.

In general, both of these genomic vectoring methods aim to create genomes that are nearly indistinguishable from natural human genomes, except that they score highly on some combination of PGSes. This article

does not focus on perils from other kinds of germline engineering, e.g. genome vectoring that incorporates transgenic or synthetic DNA into human genomes.

Precautionary foresight

If we consider creating a world-changing technology, we have an obligation and an intrinsic desire to apply *precautionary foresight*. Precautionary foresight looks ahead to the plausible future worlds that involve a manifestation of the novel technology, and then notices harms to individuals and to society that come from the technology in those possible futures.

The perils of GE (germline engineering) have to be mapped out and considered, for three reasons:

- In order to prepare, technologically and socially, to implement GE in a way that avoids and minimizes specific potential harms.
- In order to make an informed collective decision among stakeholders (such as parents, scientists, clinicians, lawmakers, and citizens in general) about what applications of GE to prohibit under what circumstances.
- In order to accelerate GE technology by truthfully and clearly assuring stakeholders that specific perils will be avoided.

This article is firmly *not* a cost-benefit analysis of GE technology. Rather, the aim is to ensure that we are aware of every major peril of GE. Thus, except as they manifest as possible bad outcomes, this article doesn't discuss:

- Benefits of GE technology.
- Questions about feasibility, obstacles to implementation, or the effectiveness of GE.
- Feelings and intuitions about GE.
- Arguments someone might make against GE.

Of course, these items are very related to bad outcomes, as discussed in the next subsection.

Naturally, in practice, our attention will focus on the perils—and other considerations—that we judge to be actually the most concerning. But the first step, undertaken here, is to makes as complete a list as possible.

Mapping major intuitions about germline engineering

Intuitions about GE, e.g. *it's weird*, aren't immediately useful for engineering or decision making, and can be slippery—difficult to pin down and comprehensively explicate. However, intuitions pretty much always point at real things that are genuinely concerning and/or worth more thought. So, there's an ongoing project to hear, explicate, investigate, and address concerns about GE.

As part of that project, this article attempts to list every single major peril of GE—i.e., any peril that's either likely, or is plausible and would be quite bad, or is something that some people are worried about. To provide some semblance of an organization to these concerns, the list is organized into several sections. Each top-level section gives a headline intuitive worry, and then the subsections describe specific outcome-based worries that fall roughly under the headline intuition. Here are the top-level sections:

- *Unnaturalness*. Child bearing is a very organic process, embedded in natural biological and social functions. GE technology is unnatural, so it might break these natural functions.
- *Destabilization*. Society works by keeping various forces in stable equilibria. GE technology might create powerful new forces, thus disrupting social equilibria.
- *Objectification*. Humans shouldn't be treated as means to an end. GE technology might promote thinking of humans as means to an end who can therefore be degraded or discarded.
- *Transgression*. Breaking society's norm against GE would tend to lead to the norm breakers and/or the norm enforcers causing harm.
- *Misalignment*. GE might result in an increased capacity of individuals or groups to affect the world, and that capacity might be directed toward ill.

There are likely perils or intuitions about GE that aren't listed, clearly explained, or resonantly expressed here, especially religious ones. If you'd like to discuss the topic, please reach out to our gmail address: berkeleygenomicsproject

Against pessimistic precautionary foresight

Toward the aim of precautionary foresight, this article lists over 100 potential harms of GE (germline engineering). If taken prima facie, this may paint a bleak picture of a future involving GE. The sheer mass of possible bad outcomes might dissuade those skeptical of GE from seriously considering that GE might be desirable on net, and might weigh down the spirits of anyone interested in furthering GE technology. Several points should therefore be borne in mind:

- The likely benefits of germline engineering are enormous (indeed, in my view they greatly outweigh the perils).
- Many of the perils are unlikely.
  - For example, I expect that the great majority of parents who use GE technology will be especially thoughtful and caring, and wouldn't objectify or pressure their children more than other parents.
  - For example, it's unlikely that a substantial portion of possibly-desirable genetic variants will be totally eliminated from the overall human genome pool by GE—at least not for quite a long time and with quite a lot of advance warning.
- Many of the possible bad outcomes would happen with or without GE.
  - One example: Both natural and assisted reproduction carry risks of miscarriage and developmental problems.
  - Well-implemented germline engineering would carry this risk for different reasons than natural reproduction, but wouldn't necessarily carry a higher risk. In fact, reproduction with GE technology might help rather than hurt: It might be possible to reliably create zygotes that have both a higher degree of epigenetic competence than the default, as well as a genetic predisposition to being exceptionally healthy despite any potential minor developmental problems.
- Many of the perils wouldn't be that bad.
  - For example, although in theory genomic engineering could decrease the amount of information gained in each generation about which genes are more or less fit, the costs of this occurring are not very high. Also, the percentage decrease would likely be quite low (even strong germline engineering would, in each child, affect less than 1% of the genetic variation between humans).
- Many of the perils can be avoided by social or individual decisions.
  - For example, we can decide to not "slip" into toxic eugenic social mores or government policies, by having a clear understanding of and commitment to genetic liberty.
- Many of the perils can be avoided via good technical development.
  - For example, the genomically-vectored stem cell or early embryo can be screened with deep whole-genome sequencing, thus avoiding any perils from DNA damage accrued in the genome vectoring process.
  - For example, through technological innovation on cost effectiveness and policy innovation (e.g. subsidies and accessibility-positive regulation), germline engineering can be made widely available regardless of wealth or class, thus avoiding an increase in inequality.
- Some of the "potential perils" listed here don't actually refer to bad outcomes.
  - For example, some people might worry that GE technology would disrupt the default process of natural selection. But many others, myself included, don't view the default process of human evolution as having especially good effects, or as being an appropriate object of strong loyalty.
- Some of the perils are somewhat contradictory, i.e. somewhat mutually exclusive, so that one can't argue that both bad outcomes are likely to happen.
  - For example, if in fact GE people end up with some health issues because of GE, then this cuts against concerns about disrupting the economic niche for doctors, and partially cuts against concerns about inequality due to GE people having a health advantage. Either some GE people have worse than average health or they are all unfairly healthy, but not both.
- In the limit of overzealous precautionary foresight, any possible bad outcome in any possible future could be listed, and somehow connected with GE.
  - As an analogy, one could imagine arguing against making a nuclear fusion reactor because maybe if there's abundant cheap energy, even more people will watch even more TV and be more unhappy. But it doesn't make much sense to blame that outcome on nuclear fusion.
  - Since GE technology would be a substantial change to a central part of life, it touches, at least a little bit, on many aspects of life. Since GE touches on many aspects of life, there is a large surface area to raise *possible* perils.
  - The important questions to be focused on are: How can we avoid this peril with technical and social innovation? Should we avoid certain applications of GE to avoid this peril? How do the unavoidable perils compare to the likely benefits of GE?

Unnaturalness

An attempt to speak from the center of this intuition:

> Influencing the genetics of our children is unnatural. For a few billion years, genes have fallen where they may, and breaking from that is a big change. The ways that we and the world are adapted to that state of affairs is both complicated and also partly unknown to us.
>
> There's a sanctity to bearing and raising children. It's in some sense the root and heart of life, so it structures everything about the world and us. Therefore, messing with the process of bearing children is messing with something at the core of life. That's not something that people can do in a way that accounts for what matters, so we should keep it as a region that's protected from manipulation. GE (germline engineering) would violate that sanctity.

What follows are more explicit, outcome-based concerns that are part of what's pointed at by this intuition. Two general types of concern are first, then more specific ones.

Chesterton's fence

A general reason to suspect risk from messing with genes, is Chesterton's Fence. The idea is that if something was put there by someone, there's probably a reason, and if you mess with it without understanding the reason, you're liable to cause harm.

Evolution selected for reproductive fitness, and so also selected for many other things we consider good, like health of ourselves and of our children. Messing with reproduction might mess with mechanisms that evolution put there, so to speak, that have important good effects when they're not messed with.

Chesterton's fence is nearby some other reasons not to mess with old things. Old things are well-tested, and so have a fairly bounded downside risk (though also a fairly bounded upside risk). Also, we understand more about the risks of old things than the risks of new things, and how to deal with those risks and take advantage of opportunities. More generally, elements within ourselves, our peers, and our world, may be adapted to the old state of affairs, and adaptedness is in general good.

In general, using external calculation to direct a complex natural system is fraught because the director is cut off from information flows that the system itself has access to. See Seeing Like A State and the Hayek knowledge problem.

Goodharting

Vectoring a genome to score highly according to some polygenic score (PGS) is an instance of Goodharting, i.e. trying to obtain a high score on a test in order to obtain something else that the test imperfectly measures. This potentially introduces several problems, e.g.:

- *An engineering target ceases to be a good measure.* The PGS may not perfectly measure the trait you have in mind. In that case, when you push far out of the normal distribution, the PGS is no longer a good measure for that trait. Basically what you've been doing, is running a search for methods to easily increase the score. If you haven't been checking whether that method also increases the trait, not just the score, then the trait might not be increased (and other stuff might get messed with).
- *The trait itself might become undesirable.* A trait that's engineered might be a good predictor of overall flourishing and wellbeing in normal humans, but might stop being a predictor of that when optimized too hard.
- *Abnormality breaks things.* You might break other things by pushing far outside the normal. (See many items below as examples of this general consideration.)

Non-normality of the child's life

Since a child with a strongly engineered genome would be far outside the normal human distribution, ze might be genetically or environmentally caused to suffer or otherwise not live a life worth living.

Technical failures (how GE might produce suffering children)

- *Incorrect polygenic scores.* Scientists who construct polygenic scores for traits might fail to account for epistases, population differences, allele count effects, confounders; might identify correlated but

non-causal variants; or might make some other mistake with data collection, statistical inference, or validation. Engineering for a polygenic score that is incorrect, besides having a smaller desired effect, might have bad effects.

- *Antagonistic pleiotropy.* A polygenic score for a trait is composed by finding alleles that positively correlate with the trait. But it may be that many such alleles will also correlate negatively with (and indeed causally decrease) other desirable phenotypes. For example, some disease-decreasing genes might affect the disease indirectly by affecting behavior. So pushing toward a very abnormally high score on some PGS may drastically decrease other desirable traits, which could cause suffering.

- *Epigenetics.* Epigenetic modifications to DNA such as methylations, as well as off-DNA material such as transcription factors, control how DNA is expressed. These controls, and in particular sex-linked epigenetic imprinting, are crucial for healthy embryonic development. Depending on the genomic engineering method used, the epigenetic state of the embryo might be abnormal, leading to unhealthy development.
  - If iPSCs are used, then there will be a large amount of loss of imprinting.
  - If the genomically vectored cells are cultured for a long time, there would likely be further loss of imprinting.
  - Some genomic vectoring methods, such as iterated meiotic selection, would produce chromosomes that incorporate both paternal and maternal segments of DNA. Those chromosomes would not be epigenomically competent without subsequent epigenomic correction.

- *Variants with invisible downsides.*
  - There may be genetic variants that have upsides that are visible to GWASes or other statistical methods, but that also have downsides that are invisible to available methods. Those variants might be selected for, providing both the upsides and the downsides; if the downsides outweigh the upsides, the child would be worse off.
  - For example, there is a variant near the ERAP2 gene that increases the risk of Crohn's disease, an autoimmune disease. However, this variant was also protective during the Black Death ("Evolution of immune genes is associated with the Black Death"). This protection might have been invisible without historical genetics studies. There might be other variants for which the downsides are actually invisible to us.

- *DNA damage.* Some GE methods involved manipulating DNA, e.g. mechanically moving chromosomes, modifying base pairs with CRISPR-Cas9, or going through many steps of meiosis or mitosis in vitro. These could cause broken or mutated DNA.

- *Unnatural DNA segments.* Some GE methods would create haplotypes that are out of distribution—i.e. that don't appear in any human—and which are therefore possibly unsafe.
  - *Base/prime editing.* Base editors edit a single base pair, and prime editors edit a short segment of DNA, less than 30 base pairs. Some of these edits might create a local haplotype that doesn't appear naturally. For example, if you edit a SNP, it could be that there are nearby rare variants that are correlated with the SNP. The rare variants would have evolved to be not detrimental with the SNP allele that they correlate with; but they might be detrimental when paired with the edited SNP allele.
  - *Breaking linkage disequilibrium.* Some GE methods break the correlations between alleles at loci that are nearby on the same chromosome. In some cases, the correlations may be adaptive, in that the two common haplotypes are both more fit than the other two uncommon "crossed" haplotypes. Depending on the strength of the linkage and the relative frequencies and fitnesses of the haplotypes, these effects may not show up in a GWAS (genome wide association study) using a linear model (or even one that allows for second-order epistasis). So a vectored genome may tend to manifest less of the background linkage, which may be detrimental.

- *Accidentally increasing homozygosity.* Some GE methods might increase homozygosity; many rare variants are detrimental when homozygous.
  - Without special care, some genomic selection methods, such as iterated selection methods, would drastically increase homozygosity by assembling genomes with many segments duplicated, leading to many detrimental double-recessive genotypes.
  - More subtly, it could be that segments of DNA that are especially high-scoring within given parents's genomes are more likely to be descendant copies of the same ancestral DNA segment,

and therefore selecting for high-scoring segments might select for homozygosity.
  - CRISPR editing methods such as multiplex base editing would naturally induce homozygosity because the editor would edit both homologous chromosomes at the same locus.

- *Vectoring for homozygosity.* AFAIK, GWASes generally don't model dominance effects. So if there are many rare trait-positive variants that are homozygous detrimental, and these are selected for with sufficient power, the resulting genome will have many more homozygous-rare (detrimental) genotypes than usual.

- *Selecting for homozygous-safe variants.* GE methods involving iterated recombinant selection would have intermediate stages where an engineered stem cell with increased homozygosity is proliferated. Homozygosities that would kill the cell or prevent it from proliferating would be selected against. It could be that such selection pressure has some deleterious effect.

- *Removing heterozygous advantage.* It's sometimes said that the modal genome would be highly fit. It seems to me that this depends on how much balanced selection there is. If there are many loci undergoing balanced selection, then if we restrict to just those loci, the genome with each genotype the modal genotype will have much fewer optimal genotypes than a normal genome. If the balanced selection is due to, say, variation in the environment, then the modal genome could conceivably be overwhelmingly likely to encounter some change in the environment that it is worse equipped to handle, compared to a normal genome.

- *Epistasis.* I.e. locus-locus interactions. GWASes generally assume additivity, i.e. they model the phenotype as a weighted sum of the counts of some alleles. There may be reasons to expect these models to be valid well beyond the observed genotype-phenotype regime, but it could be that locus-locus interactions have effects that pop up when the genome is well outside the normal distribution. Even a GWAS that adds terms for locus-locus interactions might still ignore real locus-locus-locus interactions that become relevant when optimizing.

- *Traits outside the regime of adaptedness.*
  - Many biological systems exhibit strong nonlinearities in performance that lie only somewhat outside their usual operating regime. E.g. if you can exert yourself and burn some calories to deadlift an X-pound weight, that doesn't imply that you can burn four times the calories and deadlift a 4X-pound weight. E.g. given twenty days worth of food all at once, your stomach can't just go ahead and process it, as usual, over the course of twenty days. Within the regime of adaptedness, everything works, even as things change; outside the regime, nothing works.
  - Robert Wadlow was almost 9 feet tall. He had circulation problems and died at age 22. Since, by these numbers, Wadlow was in the ballpark of $(272 - 176)/6.35 \approx 15$ standard deviations above the mean male height, his phenotype wasn't the result of normally distributed polygenic variation (which would put his rarity in the ballpark of 1 sample in more than 10^{40}); rather, he had a hormonal abnormality. Still, assuming that some of his major health issues were caused by his height rather than directly caused by the hormones, we can infer that the human developmental program can't cope with such an extreme phenotype. This could be described as a very-high-order epistasis: any given 50 height alleles have no epistasis with each other, because the circulatory system can perfectly well develop and function in a body that's a few centimeters taller than normal; but a set of 1000 height alleles all together, is in extreme epistasis with each other, in the sense that if they are all present there's a strong negative effect. Selection for a trait causing severe issues has precedent in plant and animal breeding.
  - If GE were used to select for height, there would be issues like with Wadlow. What if GE were used to select for intelligence? Some possible problems: skull problems (size, closure), blood flow problems to brain tissue, birthing problems, brain cancer (maybe correlated with neurogenesis / plasticity?), metabolic demands (glucose, material for myelination and neurotransmitters, etc.), mechanical overpacking in the brain (e.g. restricting CSF, neurotransmitter flow, etc.), interneuronal "conflict" (if humans are tuned to be near a threshold that allows exploration while avoiding intractable conflict), plaque / other waste, exhausting capacity of some shared structures such as the corpus callosum, exhausting physical room for receptors / pumps / synapse attachment, disrupted balance of ions. How likely are these? What are others?
  - Conceivably, even just removing a large number of variants which are purely deleterious in normal humans, could have this same effect. E.g., if height is controlled by many such genes, this change would make a child who's extremely tall, with the accompanying problems. It could also conceivably be the case that this genomic engineering would interfere with beneficial hormesis.

E.g. if a child is genomically predisposed to have two different layers of zer immune system both be very strong, then maybe one of the layers is so strong that it fends off almost all infections, which makes the second layer never develop properly, and then the second layer fails catastrophically when the person gets really sick.

- *Survivorship bias.* In the pipeline from primordial germ cells, to gametes, to fetuses, to babies, very many would-be offspring-contributions are lost. Often this is due to genetic mutations. Mutations that would be deadly to, say, an oocyte, would not show up in the adult population. PGSes usually measure people who were already born alive. Those PGSes will not account for variation that would have definitely prevented reaching adulthood. So, in principle, selecting too hard on such a PGS, or generally making the genome too unnatural, could drive the genome into a region that's developmentally harmful, without warning.
- *Selecting for culture viability.* Many GE methods involve making a baby from a cell that comes from stem cells cultured in vitro. Culturing cells applies selection pressures which lead to genetic aberrations.
  - E.g., oncogenes are often prevalent in culture lines. For example, culturing cells and/or using CRISPR-Cas9 (especially versions that create double strand breaks) can select for p53-inactivating mutations, which are oncogenic (see "Frequent Aneuploidy in Primary Human T Cells Following CRISPR-Cas9 cleavage").
  - E.g., some GE methods ask for culturable haploid cells. That might apply an abnormal selection pressure toward genes that make haploid cells viable in culture, with unknown effects.
  - With more effort, culture lines can be filtered to discard bad mutations, but we might not know all the relevant mutations.
- *Poor choice of traits.* Parents and/or clinics might choose to engineer traits that are not actually good, even by their own judgement. For example, imagine that a couple decides they want to have artistically creative children, so they select for low conscientiousness and high disagreeability, which are maybe correlated with artistic achievement. But the result is two creative but troubled children, and one violent psychopathic child.

Social failures (how GE children might be especially harmed by their social environment)

- *Missing local context.* GE children might lack the peers, mentors, institutions, and culturally accumulated knowledge that would appropriately nurture them.
  - Parents might have a lot of trouble helping their GE children. For example, GE children might tend to be further from the norm on various personality traits, compared to a non-GE person. Parents would therefore be less well-prepared to appropriately care for their GE child because they don't expect those traits, or because there isn't much preexisting social technology for gracefully helping children with those traits to flourish.
  - Some GE technologies would enable multi-parent babies. E.g. iterated meiotic selection could create a child with "four grandparents and no parents", and sperm chromosome selection would create a child with one mother and up to 23 fathers. Such a child would not have the typical two parents with equal genetic contribution. The resulting parenting arrangements would at least be atypical, and therefore would be less able to benefit from standard lifeways. Futher, many-parent babies might be especially likely to be insufficiently cared for because their genetic parentage is less concentrated than that of a two-parent baby.
- *Hostile broader context.* GE children might be targeted by non-person anti-abnormality forces such as anti-intellectualism (compare violent anti-Semitism), envy (compare people vandalizing Teslas), or fear.

Strain on parents

Birthing and caring for a GE child would be challenging. E.g. selecting for intelligence might select for cranial size, which would make birthing more difficult and harmful for the mother. The child might have higher metabolic needs, have difficultly sleeping, have more extreme and less regulated emotions, be more cleverly troublesome, be more difficult to communicate with, and so on, taxing the parents. In general the parents would bear the brunt of many of the other potential perils, such as hostility from other people and regret if things go wrong.

Messing with the gene pool

Decreasing genetic variation

GE doesn't necessarily reduce variation across the board, because e.g. it could increase the frequency of a rare variant. But PGS targets are likely to be heavily weighted on more common variants, because common variants are easier to correlate with traits. Applying genomic vectoring pressure to common variants would tend to decrease variation. If GE is practiced widely, it could thus weaken the ability of humanity to genetically evolve in response to a changing world. It could also lead to diseases.

- *Holstein cattle.* As an example of the power of selection, take Holstein Friesian cattle, a widespread breed of dairy cattle. There are many millions of Holstein cattle, but their effective population size is less than 100. A measure of effective population size in wild populations of various species found that usually the ratio of effective (genetic) population size to census (headcount) population size is more like 1 to 1, or 1 to 10, or 1 to 100, but almost never 1 in 10^5 or 10^6 as with Holstein cattle. (More detail and thought would be needed to see the implications of this for human GE. But we see that at least one real-world breeding program has produced an extremely abnormally low effective population size.)
- *Selecting against invisibly heterozygous-advantaged variants.* E.g., a mutant HBB gene is neutral or slightly harmful when heterozygous in normal environments, is very harmful when homozygous (sickle-cell anemia), but protects against malaria when heterozygous. If that variant shows up as mildly negative in a GWAS in a non-malarial population, and then is selected against by GE, the population would become more vulnerable to malaria.
- *Linkage disequilibrium blowup.* Even without being directly selected against, a variant might be eliminated by coincidentally not being present on DNA segments that are strongly selected for. For example, if chromosome selection is widely used, chromosomes that score extremely highly on whatever PGS is used will be propagated to a great extent, and variants not appearing on that chromosome will be driven down in frequency.
- *Increasing population homozygosity.* Most GE methods will strongly select for certain segments of DNA, making those segments very abnormally widespread. Subsequent generations would then be at much higher risk of large amounts of homozygosity. This might be especially bad if the GE selects for rare variants that are very deleterious if homozygous; even if the GE method can orchestrate that those variants only show up heterozygously, it still could greatly increase their raw frequency and hence greatly increase the chance of very deleterious homozygosity subsequently.
- *Prematurely eliminating net-bad variants.* Hypothetically, there may be genetic variants that are genuinely universally net-undesirable (e.g. a variant that causes a child to suffer and die), and yet have some positive aspect to them. For example, maybe there is a variant that makes a protein much worse at its main function, but a little better at another function. If GE is very widespread, those variants could be eliminated before being studied, precluding the possibility of learning about the partial benefits of that variant (which could for example turn into a non-germline therapy for cases where the variant's advantage would be especially helpful).
- *Using up variation in unmeasured traits.* If a potentially desirable trait isn't measured, the genetic variation associated with that trait might be invisibly selected away when selecting for other traits. For example, some traits such as personality traits might have a genetic basis involving more epistasis, making those traits harder to correlate with genotypes; in the long run, there might be less variation in such traits.

Decreasing phenotypic variation

- *Selecting away weirdness.* By their nature, PGSes derived from the usual sort of GWAS will entirely or almost entirely ignore weird people. If those weird people use GE, then in general the use of GE shrinks the weirdness. For example, there could be some epistasis that makes people have sort of quirky phenotype that's valuable in some way to that person or to others. That epistasis probably wouldn't show up in GWASes, and then might be selected against very strongly (if each individual component is low-scoring on some PGS).
- *Discarding dimensions of variation.* For example, it might be that intelligence has relevantly more than one dimension, and it might be that selecting for measured g-factor selects against variation in some of those dimensions. So the resulting GE children will all have the same kind of intelligence, and

problems in the world that are much more profitably addressed with some weird kind of intelligence will go unaddressed.

- *Converging on "optimal" points.* Depending on the kind and power of GE, it might produce children with a fixed genome or small set of genomes. For example, chromosome selection, depending how it's used, could use up all the available inter-chromosome variation in one generation, with nowhere further to go.
- *Replacing beneficial diversity with a single average good point.* If people mostly target a single desirable level for some trait, then variation in that trait that's beneficial in the aggregate could be decreased. For example, perhaps the desirable average disagreeability is fairly low, so that there is social harmony and cooperation. But having many people who are somewhat more disagreeable is also a good, e.g. because those people might disproportionately drive some kinds of intellectual progress.

Promoting harmful genes

As described above, some GE methods might create people who have some unnatural haplotypes (e.g. due to base editing, or crossover at abnormal points). If those people have children, they might pass on some of the unnatural haplotypes to the next generation. The haplotypes, which might be harmful, could then spread into the gene pool.

Separately, GE could create people with many genes that turn out to be generally undesirable—e.g., if there are health problems associated with IQ, and many GE children have genomes that are heavily vectored for IQ. If GE is widely applied in this way, then there would be many people with increased numbers of alleles that turn out to be harmful. Those alleles would thus be more frequent in the overall population, so that subsequent generations could have higher rates of the associated health problems.

Blocking the flow of information coming from natural selection

Natural selection—the filters on surviving, thriving, and mating that determine which organisms reproduce with which organisms—induces a complicated, changing breeding structure that takes many aspects of organisms into account. This process can be viewed as pumping information into the gene pool. Germline engineering cuts off this flow of information to some extent, replacing it with pressure on human-measurable features. So if GE is widespread, then the "knowledge" present in the genome pool about which variants are generally fit is, along the dimensions that GE is applied to, frozen at whatever information is already present in PGSes.

Harm to animals

Some GE technologies would benefit from animal experimentation, including observing adult GE animals. This could cause animal suffering by creating malformed animals. Also, GE technologies might be used to create more efficient farm animals, which could in theory cause a Jevons effect, e.g. increasing the total number of individual cattle farmed even though each individual cow produces more.

Destabilization

An attempt to speak from the center of this intuition:

> Things are going to get really weird once there are enhanced people. It'll change the way people look at each other, enhanced or not; and there will be many people acting in ways that were previously very abnormal. In some ways, society is already bursting at the seams with social forces and changes. With enhanced people in the mix, these social forces and changes will only get more volatile.
>
> To say it another way: Current social institutions—formal organizations, behavioral norms, social roles, economic flows, structures of trust—are adapted to the current distribution of genomes. Both by conscious design of institutions, and by gradually coping with local reality, people have co-adapted their behavior to work well with the behavior of other people. Germline engineering would change people's behavior, and would also change people's expectations about other people's behavior. Those changes might, at least temporarily, disrupt people's co-adaptations, causing social equilibria to destabilize, lose capacity, or disintegrate.

To elaborate a bit, GE could cause some of the following changes in the population of humans:

- The distribution of phenotypes changes in general.
- More specifically, the distribution of phenotypes diversifies and/or extremizes, so that for example there are many more people with some of the following traits:
  - very good health,
  - very high attractiveness,
  - extreme personality traits such as disagreeability or persistence,
  - or very high cognitive capacities such as IQ, charisma, empathy, verbal ability, artistic creativity, technological and scientific ability, ability to manipulate people, and so on.
- The distribution of phenotypes becomes bimodal: there are non-GE people and there are GE people, as two distinct and separate clusters.
  - For example, GE people are likely to be healthier, perhaps much healthier, in general, compared to non-GE people.
- The distribution of GE phenotypes undergoes splitting: there emerge multiple distinctly separated groups of GE people, differentiated by what traits they do and don't target or manifest.
- The distribution of phenotypes goes outside the human realm on some traits. E.g., there are people who are smarter than anyone who's ever lived.
- The distribution of phenotypes starts to include some people who lack core aspects of humanity, such as empathy, shame, language, or love.

Separately from whether those changes happen, there might also be a widespread perception that such a change has happened. For example, even if GE people are in fact quite diverse, non-GE people might view GE people as a coherent and separate class of people. These perceptions, however true or false they are, could on their own affect society via downstream actions such as discrimination.

Removing the technical infeasibility excuse for parents

Currently, parents might be blamed for raising their children in a way that some other people consider inappropriate; on the other hand, parents cannot reasonably be blamed for not using GE to have children, because they cannot currently do so. If GE existed, that excuse would be removed, so parents might be pressured to use GE, impinging on parents's procreative liberty.

Breakdown of trust from fear of manipulation

Some normal people might think (correctly or not) that there are people with enhanced cognitive abilities, such as intelligence, empathy, or charisma, and that those enhanced people are able and willing to manipulate (deceive, coerce) normal people. Those normal people would then mistrust both enhanced people, who might manipulate them, and also unenhanced people, who might have been manipulated (perhaps imperceptibly) by enhanced people.

Inadequate social norms

Social norms are a form of technology—they have to be invented, tested, refined, and spread, so that they work well given the people applying the norms. If there are many GE people who have personality traits that are distributed differently from non-GE people, some existing social norms might no longer work to make living together go well. It may take time to create new satisfactory norms, and in the interim people could be harmed by the lack of satisfactory norms.

For example, if there come to be many more people with fairly high disagreeability, coordinating on many-person tasks might become much more difficult. Conversely, if there are many more people with fairly high agreeability, those people might be easily manipulated into harmful mass actions, or might be easily exploitable, or might tend to not get their needs met.

Breakdown of empathy

If the average difference in personality traits between people becomes much larger, it might become much more difficult for most people to empathize with each other. That could cause, for example, more social friction, more political friction, more fragmentation in society, more loneliness and difficulty forming relationships, more difficulty in coordination, or more difficulty in giving and receiving mental health support.

Loss of human dignity

Human dignity is something afforded equally and intrinsically to every human, which separates them from other beings, and makes them deserving of a respect and care that is special to humans.

As discussed above, GE could change the distribution of phenotypes in general, or specifically so that it's more diverse or extreme, or so that there's a distinction in kind between GE and non-GE people, or so that there are humans who are significantly outside the normal human envelope of phenotypes. Those changes could blur the lines of humanness. Even if GE does not actually significantly blur the lines of humanness, in that there is a good notion of humanness that does still identify all humans, GE could still make people believe that the lines are blurred.

If what constitutes being a human is unclear, then respect for human dignity might be harder to deploy as a foundational social stance. E.g., it might be less immediately obvious to everyone that any human-descendant in a medical emergency deserves help. Further, widespread GE might reinforce viewing and treating humans as mechanical objects, which might decrease the social commitment to human dignity.

The following subsections elaborate on some possible consequences of the real or perceived degradation of a clear universal idea of humanness.

Escalating coalitional conflict

GE people might be categorically stigmatized as such by non-GE people. Likewise the reverse, if GE people form a community. The stigma could escalate into active hostility, from kids bullying kids to job discrimination. If it escalates enough, it could become a violent conflict.

Further, the conflict could be created merely from the expectation of its possibility, plus uncertainty about the other side's current stance. If non-GE people expect GE people to form a coalition that's adversarial to non-GE people, the non-GE people might preemptively coalesce to disempower GE people. Likewise the reverse: GE people might preemptively disempower non-GE people.

Likewise, coalitional conflict could develop from splitting scenarios, where different groups of GE people view themselves as coherent, distinct, and opposed.

Centrifugal force on marginalized people

If some traits become much rarer, people with those traits might be generally left in the cold. Those people might prefer to be a part of a community of other people who share the trait. In that case, they might become more and more separated from the center of mass of humanity, creating a split.

Breakdown of collectivity

Collective projects rely on a sense of community and an expectation of communal benefit. A key aspect of human dignity is membership in the total moral, political, cultural, and economic community of humanity. If that membership status is unclear for many people, then the expectation and pursuit of a communal benefit might be dispersed, in the same way that racism can divide a country against itself. Example of community elements that could be threatened:

- Equality before the law. In general, justice through universally applied rule of law.
- The humanistic scientific project, wherein human capacities to grow, understand the world, and co-create the future are highly valued and invested in, partly because they will benefit future humanity in general.
- Communal force behind norms, where people follow norms because they value being part of the community that would reject them if they broke the norms.
- Patriotism, i.e. loyalty to and investment in the community of all citizens of one's father land, which motivates national projects such as infrastructure, welfare, education, and research.
- Peace through negotiation, cooperation, trade, and treaties, rather than through war and domination.

Depleted occupants for social/economic niches

If very large numbers of people use GE, there may be traits that become the new norm. If the newly normal traits are somewhat incompatible with performing some social role, that role might go unfilled.

For example, some jobs are especially intellectually unstimulating. If everyone had a much higher need for intellectual stimulation compared to the population today, there might be no one to do unstimulating labor—or in other words, the minimum amount of painful boredom required to do those jobs would increase.

Another class of examples comes from roles in communities of atypically-abled people. For example, if there were orders of magnitude fewer deaf people, there might be fewer or no sign language teachers or teachers specialized in teaching deaf children.

Depleted resources for some people's needs

Some traits mean that a person would benefit from some special care, such as healthcare or assistance, and would have a worse life without that care. E.g., a deaf person might benefit from hearing aids or implants. E.g., someone with a specific illness would benefit from treatment.

If some condition is mostly preventable by GE, there may be many fewer people born who will have that condition. In that case, the people who either already have that condition, or who are born without using GE to avoid the condition, might have their lives made worse because they'll have fewer available resources (such as scientific investigation of the condition, technological development for treatments or assistance, community building, or government welfare).

The decrease in resources could happen simply because there are fewer such people. Separately, it could happen because people who are born in the condition, or their parents, could be viewed as blameworthy for not preventing the condition. The reasoning might go: Why should the rest of us help people in this condition, when the condition could have been avoided? Similarly, the reasoning might go: Clearly we value not having this condition, because most of us choose to prevent it; so it is at least to be considered a disease condition; and so we will not treat this condition as an equally admirable condition compared to typical alternative conditions.

Disrupted social/economic niches

Generally, GE would cause large changes in the world, and therefore might disrupt economic niches. E.g., doctors might become unemployed because everyone is very healthy.

More specifically, if there are many people with high ability to advance science and technology, there might be extreme material abundance. The rate at which jobs are obsoleted or automated might greatly increase.

Without a politically viable way to distribute resources, many people could be left without much economic opportunity for a more flourishing life. Further, without bonds of interdependence between people imposed by the cooperative struggle for material resources, people might become very isolated from each other, as is already happening.

State conflict

States might go to war to prevent the use of genomic engineering in general, or in specific applications viewed as abhorrent or threatening. They might also race for germline engineering technology, potentially causing them to cut corners on safety or push too far.

Further, if some states use GE, and that is viewed by other states as a major transgression, then other international norms might erode, such as the norm against developing and deploying nuclear weapons.

Disrupted gender relations

One of the main reasons that women and men form love relationships is in order to bear and raise children. Some component technologies of GE, such as in vitro gametogenesis and artificial wombs, would enable women to have children without men or men to have children without women. If that ability thus removes one of the major stimuli toward women and men forming love relations, those love relations might become significantly rarer, more unstable, and more difficult.

Unequal access

GE could stay inaccessible to many people:

- It might be expensive due to the underlying difficulty of the technology.

- It might be expensive and/or regulatorily restricted and/or banned in some jurisdictions, e.g. because a majority of citizens want regulation or because the purveyors of the technology regulatorily capture the sector.
- There might be some ancestry groups for whom polygenic scores for various traits are not constructed, e.g. because of expense or because there aren't enough people.

At the same time, GE technology might be accessible to other people. E.g., regulation in most jurisdictions would still let the very wealthy access the technology on an island or something.

If only some people have access to GE technology, inequality would be increased, which would be unjust. There could be conflict between those with access and those without.

Objectification

An attempt to speak from the center of this intuition:

> Children aren't objects with dials and buttons to measure and tune; they aren't machines, and they can't be calculated. Children are ends in themselves, not means to an end. GE technology thinks of humans as objects, which would make it ok to degrade or discard them.
>
> To say it another way: Genomic engineering takes humans and humanity as objects to be manipulated. This cuts off the relating-to that's necessary to deal rightly with other beings that are the same sort of being as you; the empathy, the openness to co-creating language and ideals, the willingness to be moved by negotiation, the care for them for their own sake, the enjoyment for its own sake of interacting with another. Making humans the target of strong optimization pressure both incentivizes and socially evokes optimization pressure that treats humans as instrumental, which unjustly suppresses respect that should be shown toward the self-sovereignty of the internal locus of agency of each human. That harms humans who are treated that way, and creates conflict with them. Further, parents shouldn't, and don't want to, think of their kids as things to optimize.

Consent

Children can't give prior consent to being created. GE is in some ways more risky than natural childbearing, and GE is a deviation from the natural state of affairs. So consent is more of an issue with GE. (More so, to the extent that the necessity of consent depends on deviation from a prior default or natural state of affairs.)

Removal of ascribed agency

People might think that a GE person's genome determines that person's behavior to some large extent. This perception might be strengthened by people seeing the world invest in GE and seeing the results of GE.

This perception could lead to people (GE or non-GE) assigning less blame to GE people for their harmful actions, and/or less credit for their helpful actions. Inappropriately treating GE people as blameless could make them behave worse. Inappropriately withholding credit from GE people could make them less motivated to do helpful things, and could make their lives worse by depriving them of social acceptance.

Harm involved in conscription

GE children might have high capability in some domains, and so might be especially targeted for conscription in general. E.g.:

- conscription by governments into literal wars or other conflicts,
- conscription by ideologies into missions,
- conscription by social class into class conflict,
- conscription by non-person emergent social forces into self-reinforcing non-person behavior, or
- conscription by parents or local social context into some specific life path.

Conscription in general involves harmful behavior such as deception, punishing agency, withholding help, threats, isolation, sacrificing epistemics in favor of superficial coordination, "pointless" harm to reinforce surrender mindsets and cripple direct capacity to resist, applying these tactics to people related to the target, and controlling in general. So GE children might be especially targeted for harm.

Less intensely, but more likely, GE children may be socially pigeonholed, and may be socially pressured to take on tasks. This restricts their freedom.

Deficient social context of intrinsic care

Parents who use GE for their children might be selected for treating children as means to an end rather than ends in themselves, or for being in a local social context that does that.

Also, the act of using GE might *cause* parents or their social context to place value on a child's life because of the instrumental value of the child, rather than for the child's own sake. By providing social proof that communicates "our values are whatever would have recommended to use GE", using GE might implicitly reinforce that a child is worthwhile and worthy of care because of the traits engineered for, and perhaps implicitly *not* because of the child's own experiences and values. A social context like that could leave the child starved of what is called love, acceptance, and security.

Moving the Overton window toward eugenics

Due to the horrors of Nazi Germany, as well as early 20th century eugenics (mass forced sterilizations, racist laws), society has erected a socially-enforced mental wall to prevent people from gathering political will around coercive eugenics. The mental wall might not be able to make subtle enough distinctions to allow parents to individually, autonomously choose to use GE technology, without also allowing coercive, population-targeted eugenics.

Promoting racism

Visible successes of GE technology would demonstrate that there's a significant genetic component to human behavior and capacities. Apparently there exist people who think the genetic component of behavior implies that various groups of people should be abused in various ways; such people could thus be emboldened by GE's successes.

Sacrificing well-being for competitive advantage

To make genes controllable is also to make GE an available move in competitions. GE to win in a competition may select against well-being by selecting in favor of traits like single-track thinking and self-sacrifice. Competitive pressure to increase genomic vectoring power could drive people to cut corners on safety, resulting in suffering GE children.

Making society overly prioritize technologically optimizable traits

On the one hand, there is a desire to apply some technology. On the other hand, there is the structure to fulfill that desire—the scientific and technical knowledge, the legal environment, the social norms, and the social institutions. The desire, and the structure to fulfill the desire, reciprocally cause each other: The desire motivates people to develop the necessary structures, and the presence of some structures makes it easier to design the remaining structures and coordinate to implement them.

In this way, making it feasible and inexpensive to strongly genomically engineer some trait might make society desire and/or pursue that trait more than would be good. E.g., being able to select for intelligence could make society value intelligence over morality; as in, "we don't need to worry about raising kids to be good people because we can just make them intelligent".

Making society deprioritize non-GE children

By a similar token, if people think that GE children have qualities that make them worth investing in, they might uninvest in non-GE children. This would be especially bad if parents themselves treat their GE and non-GE children differently. Further, non-GE kids may feel resentful of their GE peers, or may feel less deserving than them; this might happen even if the GE kids aren't actually treated differently, but just because the pervading ideology seems to imply that GE kids are more worthwhile.

Making society unsupportive of surprising behavior

GE could reinforce thinking of people as optimizable objects—machines with a correct mode of functioning, where surprising deviation is bad and to be corrected. This cuts against the "openness to the unbidden" that's necessary for communities to hold toward children.

Fetishizing traits or genetics

Some people incorrectly attribute desirable concomitant qualities to traits such as intelligence in a rigid way that is not suitably responsive to evidence. Likewise, some people rigidly assume that a person's genetics very strongly determine that person's traits or behavior. Those stuck beliefs may cause them to be reckless with GE technology, and to have incorrect assumptions about how to interact with GE children and what to expect from them.

For example, such a person might rigidly assume that a child genetically predisposed to be intelligent will be creative, curious, clever, and compassionate, without guidance; and they might fail to notice that the lack of guidance is the issue, instead blaming the child for not realizing the potential that is surely there.

Making reproduction artificial and clinical

Nearly all GE methods involve fertilization through some method other than sex. If GE were widespread, it would sever the link between sex and reproduction. This could contribute to people thinking of children as objects rather than people. Also, it could make reproduction more unaesthetic and unerotic compared to natural reproduction, and could disrupt relationships that would otherwise have been strengthened by that shared experience.

Killing embryos

Some GE methods would involve creating many early-stage embryos, most of which would be discarded. Many people would strongly object to that practice because they view embryos as human lives worthy of protection. Also, GE technology in general could further shift society toward not treating any embryos as lives, e.g. by placing fewer restrictions on abortion.

Transgression

An attempt to speak from the center of this intuition:

> Manipulating the genes of future children is not something that society accepts, and doing things that society doesn't accept causes harm. People who decide to do such things can't be relied on to actually do such things beneficially.

A theme in this section is the Unilateralist's Curse. Because there are strong social forces pushing against developing and using GE, the first people who choose to do so anyway will tend to be atypical in some way. Some atypicalities will tend to make those people develop or use GE in a more harmful way than average.

Punishment

- *Parents, scientists, technologists, funders.* People involved in doing GE might be punished by reputational damage, loss of jobs, loss of influence, harassment, violence, stigma, sanctions, fines, or imprisonment. For example, He Jiankui and his collaborators were fined and imprisoned after "widespread criticism" for using CRISPR/Cas9 to edit out a gene from two twin girls to protect them from HIV. (His experiments were indeed dangerous and irresponsible.) Steve Hsu was made to resign from an administrative position (though retained his tenured faculty position) due to protests about his discussion of the genetics of intelligence. This might spill over to other projects; e.g. if a funder funds both GE and cultured meat research, then cultured meat research might suffer reputational damage "by association" through the funder.
- *Children.* GE children might be stigmatized and treated poorly by institutions, e.g. having their citizenship revoked/denied.
- *Future GE, other biotechnology.* A GE project that goes poorly might cause backlash and legal restrictions, making it more difficult for future GE projects to succeed. This might spill over, so that other related biotechnologies such as IVF, IVG, adult gene therapy, artificial wombs, GE in animals, and so on, are also restricted or banned more than they'd have been otherwise.

Criminality

- *Keeping secrets.* Because of the threat of punishment, people who work on GE might be pressured to keep secrets. Keeping secrets pressures people to lie, and creates a social context that makes it easier

to behave harmfully because there's less oversight. Keeping secrets makes people expect to be lied to and expect to not be able to resolve contradictions, so it makes it harder to have a truthful, sane shared social reality that produces good decisions around GE.

- *Selecting for and evoking criminality.* People or larger organizations who work on GE are selected for being willing to break taboos and/or laws and/or international agreements, and to avoid responsibility and oversight. Also, by breaking taboos or laws or agreements, people might bond through transgression and imply in implicit common knowledge that "transgression is what we do". So GE might be predisposed to be misused, and GE children might be around people more disposed to behave in a harmfully transgressive way.

Fanaticism

In the same way that people who work on GE are potentially selected for criminality, they're also selected for having very strong motivation, strong enough to overcome the avoidance of transgression and to spur difficult feats of bioengineering. Ideology (group-reinforced stories about overarching meaning) and other strong motivators might spur people to be reckless with GE, e.g. by not being cautious to avoid creating suffering children or by trying to use GE to gain power rather than to achieve life-increasing ends.

Hubris

Similarly, people who work on GE are selected for not worrying much about the consequences, and for being overconfident about the positive effects—"playing god". So they might be uncareful in applying the technology. For example, they might:

- …not apply sufficient checks to the genomic and epigenomic integrity of the cells they attempt to make babies from.
- …downplay the risks and overplay the benefits to parents, regulators, and/or investors.
- …not exercise good judgement in which traits to refuse to genomically vector for.

Misalignment

> The human capacity created by GE might be directed by values that we don't like. And the creation of GE people might negatively affect how all human capacity is directed.

Intentional misuse

...of component technologies

In developing GE technology, other technologies might be developed that could be dangerous by themselves. I'm not aware of many of these for GE, and would like to know if there are more. Some hypothetical examples:

- *Viral vectors.* If novel viral vectors are used to deliver DNA into cells, those viral vectors might threaten accidental or intentional viral outbreaks.
- *Genome synthesis.* This could be misused to create pathogens.

...of GE technologies

- *Fraud by GE providers.* Apparently multiple doctors have used their own sperm to sire hundreds or thousands of children without parents's consent.
- *Selection for usability.* Conceivably, a government, or other large organization such as a social movement, might create GE children selected for traits that make them useful as tools for the organization, such as obedience or willingness and ability to do violence. This would make the GE children potentially harmful and/or take away some of their agency.
- *Selection for difficult atypicality.* A deaf couple intentionally selected a deaf sperm donor so that their child would be deaf. Other parents might want to use GE to have a child who has blindness, dwarfism, or some other atypical trait that, prima facie, gives zer a life that is more difficult in at least one major respect.

- *Selection for values.* Apparently, a wide variety of central political attitudes have substantial genetic components, and likewise for personality traits ("The genetics of human personality", Sanchez-Roige et al.). Parents or governments might select children to hold certain attitudes or have certain personality traits. In many cases this would influence the center of mass of the values of humanity in a seemingly non-epistemic or unfair way, and would take away agency from the children.
- *Competitive selection and inequality.*
  - (Cf. the Objectification section.) To make genes controllable is also to make GE an available move in competitions. A competition over genes could, Moloch-style, emergently lead to outcomes no one wants.
  - E.g., selecting for tendency to gain power or money, might select in favor of sociopathy, single-track thinking, non-epistemic charisma / persuasiveness, and so on, which could lead to a world that's not desirable to live in for any of its inhabitants, as in The Rapacious Hardscrapple Frontier.
  - E.g., selecting for height and other traits associated with attractiveness or athletic performance might create a zero-sum escalation.
  - Such a competition could make the world even worse for people who don't want to or don't have the resources to select for competitiveness. Even if the world has some people who are living worthwhile lives, many or most people could end up left behind and excluded from gains.
- *Selection for harmful behavior.* Some couples might select for traits that increase the likelihood that their child will harm others. E.g. high disagreeability, low conscientiousness, low obedience, high charisma, low empathy, dominance, sadism, pride, shamelessness. Likewise, they might select against helpful behavior, such as altruism and scientific ability.

...of technologies developed by GE children

Free GE children might use their capabilities to develop technologies that are dangerous. Even if the GE children don't have any intention of doing harm, those technologies might be misused by others. In other words, GE children might increase the speed and volatility of technological development without much increasing the overall wisdom of humanity, and since technology tends to spread, that might greatly increase the total amount of unwise use of technology.

E.g., more technology in general could lead to more consumption and destruction of the environment. E.g., more insight into artificial intelligence might lead to the creation of a world-destroying AI system.

...of trust in reported phenotypes

A person might try to deceive measurements of zer phenotypes in order to cause other people to select for or against zer genes. E.g. ze might lie about income, health history; or ze might cheat on physical or mental tests.

Accidental misuse

Unmapped effects of traits

Even if a trait is accurately measured by a PGS and successfully increased by GE, the trait may have unmapped consequences, and thus may be undesirable to the parents and/or to the child. For example, enhancing altruistic traits might set the child up to be exploited by unscrupulous people.

Poor communication with decision-makers about traits

For whatever reason—incompetence, the intrinsic complexity of the topic, fraudulent deception, or disinterest of the parents—salespeople and clinicians might misinform parents about the nature and consequences of traits. That might cause the parents to choose traits that aren't what they would have wanted if better informed, and that are bad for the child's wellbeing. Further, the parents might therefore be taken off guard by the results of GE, and be less prepared to appropriately care for their GE child.

Conscription

The film Gattaca (1997) depicts a world with widespread genomic engineering, where people with high-scoring genomes are conscripted into a social class that excludes and mistreats the non-GE people. Huxley's Brave New World depicts a similar class dynamic enforced with coercive population eugenics, poisoning

babies, drugs, sexual abuse, and strong norms against thinking. Whatever intelligence can survive that state of affairs, is put toward maintaining it.

More generally, governments, ideologies, classes, and other coalitions (including whoever develops GE technology) might deceive and/or coerce GE children into fighting on some side in a conflict. This takes away agency from the children, reinforces conflict, and helps coercive forces thrive.

Even more generally, one might think that humanity as a whole has net-bad motivations by default, i.e. wants to do things that are bad on net. If so, then empowering humans is bad on average because it enables them to do more of what they want to do, which would be bad.

Enabling socially enforced eugenics

If GE is available, society might pressure parents to use GE rather than not, or to use GE in certain ways that align with what society wants but not with what the parents want. For example, society might pressure a deaf couple to prevent their child from being deaf, whereas the deaf couple might want to leave it up to chance or make their child deaf.

This is a kind of eugenics—society exerting its collective will to override individual genetic liberty—and therefore would cause many of the same harms as historical eugenics. E.g. society might believe some GE application is desirable but actually it is harmful, and then very many GE people are given the same detriment in tandem. E.g. society might want to erase some kinds of people, perhaps because they are viewed as a burden, or out of hate.

Internal misalignment

- *Antagonistic pleiotropy with unmeasured traits.* Some crucial traits, such as what is called Wisdom and what is called Kindness, might not be feasibly measurable with a PGS and therefore can't be used as a component in a weighted mixture of PGSes used for genomic engineering. If there is antagonistic pleiotropy between those traits and traits selected for by GE, they'll be decreased.
- *Traumatizedness.* Due to potentially being abnormal, invidious, conscripted, or around harmfully transgressive people, GE children might be traumatized and then therefore harm others.
- *Antagonistic coalition of enhanced humans.* Humans selected to have very high physical or mental capacity might, by their nature, be misaligned with the values of the rest of humanity. In some cases that would be good, since humans selected to be intelligent will predictably make moral progress. But, for example, it could be the case that when humans grow up depending on other people in the normal way, they grow up to be kind and able to relate with others; but if they are supranormally capable and don't have to depend on or work with others, they grow up to be cruel and isolationist. In that case, highly enhanced humans would be a danger to what we care about. Intrinsic misalignment is also related to intuitions about being "left behind" by GE; not only can they outcompete the non-GE people, but they might not care about non-GE people. Also, enhanced humans might engage in runaway assortative mating strategies, meaning that they progressively decrease mating with non-GE humans; reproductively isolated populations might (be feared to) have their values less coupled with the values of the rest of humanity.

Destiny change

Generally, by changing what sort of humans exist, GE would change what humanity is, where it is going, and what forces determine where it is going. That change could be a change for the worse.

Disruption of natural selection

One might think that there's a sort of god of humanity, constituted by default-human-evolution as it has been happening up until now. In this view, the default process of natural selection will select for fitness, which is goodness; humanity is thus improved over time. On such a view, GE would be bad because it would disrupt natural selection.

Similarly, one might think that it's good for some people to have children and others not, because that reflects the values of humanity as expressed in mate choice. On such a view, GE would be bad because it would disrupt the "soft eugenics" of mate selection.

Shifted distribution of values

GE people might have a significantly different distribution of personality traits from non-GE people. That might constitute a change of values. For example, being less compassionate might imply a smaller moral circle. Assuming GE people have a voice in the future of humanity, their differently distributed values would change the center of mass of humanity's values.

Hypothetically, with more extreme applications of GE, some GE people might be created who are missing major cognitive elements, such as a sense of fairness. This could constitute a large shift in humanity's values.

Erasure of some kinds of people

One might think that the current variety of people is a better starting point for the future progression of world-society, compared to the variety of people that would result with GE.

For example, one might think that even phenotypes that some would consider undesirable—e.g. autism, or schizoidness, or ADHD, or deafness, or blindness, or dwarfism, or transness, or paraplegia—represent an important element of humanity as a whole. If GE would greatly decrease the fraction of a phenotype, then the unique elements provided by that phenotype would be robbed of their contribution to determining humanity's destiny.

For example, if autists can integrate some kinds of information more powerfully, or schizoids can think in useful uncommon ways, or the blind can perceive sounds and touches with more depth of understanding, then those ways of being have something to offer which would be lost without such people. Without those elements, humanity's collective understanding and abilities would be perhaps diminished, or at least altered in emphasis.

Beyond that, any phenotype at all will correspond to some kind of consciousness. Someone with insomnia, even if they acknowledge that having insomnia is almost entirely worse than not having insomnia, might still wish to have other people with insomnia to be friends with, simply because an insomniac has a somewhat different experience and way of being than a somniac and can therefore understand and relate specially to insomniacs. So removing any type of person is to some extent changing who humanity is.

Finally, a given type of person (so to speak) might view themselves as part of a "cross-sectional coalition". In other words, even though a deaf person is not *only* a deaf person, and views zerself as part of the whole human collective, ze might also view zerself as being part of a narrower collective—deaf people—which has its own being, rights, authority, autonomy, instrumental value, and destiny.

Diminution of affinity groups in general

Besides the loss of any given type of person described above, GE could cause a partial loss of participation in affinity groups in general. People like to be in tribes. If some kinds of variation (such as diseases) are largely removed, tribes that would have been based on the removed variation are also removed. If there's overall less basis for forming tribes, then there might be overall significantly fewer tribes. Going from participating in tribes to not participating in tribes would change a fairly fundamental aspect of being human.

Conflict over destiny

If people view the future of humanity's genome pool as a kind of territory, there could be organized conflict over what genes to promote and demote.

Loss of meaning from abundance

It's important for humans to have some measure of individual authority over the future. GE might be so effective, and the resulting world so abundant, that even assuming everyone's material needs are provided for by a collective agreement, there could still be all the problems of extreme abundance. Specifically, without the great challenge of struggling against scarcity, some people might not have a sense of authority over their future: it doesn't matter what they do, since they'll be provided for anyway. This would be exacerbated for people who aren't enhanced, even if enhanced people are protecting and providing for them.

The ease disease

Some traits that prima facie would increase human capacity might actually decrease human capacity because they remove a need for small-scale struggles, and without smaller struggles the larger struggles will be out

of reach. For example, someone who isn't especially curious but is very clever—can quickly solve logic problems—might not learn to investigate because ze can solve most basic problems easily and therefore doesn't need to investigate. Likewise, naturally healthy people might not learn to treat their body well; in principle this could even lead to worse lifetime health outcomes compared to non-GE people.

Conclusion

There are many potential perils stemming from human germline genetic enhancement. Advocates for germline engineering should understand, acknowledge, and account for these perils. Scientists and technologists should be aware of these perils and of how to avoid them through careful, ethical, responsible implementation. Likewise for regulators and policymakers. To make this world-changing technology go well, we want to hear the intuitions, wisdom, and voices of everyone, though we will not unconditionally defer to those voices. We also don't want to delay the benefits. Therefore we will move forward while working to better understand the perils and how to avoid them.