

Taking Exception to Human Eugenics

Frederick P. Roth^{*,†,‡,1} and John Wakeley^{§,1}

^{*}Donnelly Centre and Departments of Molecular Genetics and Computer Science, University of Toronto, Toronto, Ontario M5S 3E1, Canada, [†]Lunenfeld-Tanenbaum Research Institute, Mt. Sinai Hospital, Toronto, Ontario M5G 1X5, Canada, [‡]Canadian Institute for Advanced Research, Toronto, Ontario M5G 1Z8, Canada, and [§]Department of Organismic and Evolutionary Biology, Harvard University, Cambridge, Massachusetts 02138

ORCID ID: 0000-0002-6628-649X (F.P.R.)

We are concerned that the *Perspectives* article “Mutation and Human Exceptionalism: Our Future Genetic Load” by Michael Lynch (2016) opens the dark chapter of eugenics without clearly reading it as a cautionary tale.

Given the history of eugenics, especially high standards for scholarship, sensitivity, and attention to historical context are needed when discussing the complex issues surrounding human genetic improvement. Statements similar to those Lynch makes in his article—which in the 1920s and 1930s were being made by leading population geneticists such as R. A. Fisher, J. B. S. Haldane, and H. J. Muller—led directly to eugenic policies and were later readily attached to the genocidal programs of Nazism (Kevles 1995). Failing to engage these issues, or offering vague recommendations, invites misappropriation by those who wish to see the return of an aggressive eugenics.

Lynch focuses on the rate and long-term consequences of deleterious mutations in humans. Despite concluding that humans are unexceptional in both germline and somatic mutation rates, he worries that deleterious mutations might accumulate in the future because of “exceptional” human behaviors that “thwart selection.” Specifically, by treating disease and reducing variation in the number of children per person, we reduce the impact of genetics on survival and procreation, and in turn threaten the “future of the human gene pool.”

Lynch contrasts deleterious mutations of large effect, which can be detected in parents or early-stage embryos (then “culled”), with mutations that are “impervious to detection” but have selective effects that can be ameliorated by medical intervention. We will refer to these as type 1 and type 2 mutations, respectively.

For type 1 mutations, Lynch quantifies the effectiveness of culling “in which a fraction f of the population is accurately screened for the mutation, with carrier chromosomes being culled upon detection.” He does not restrict this statement to prenatal screening, referring also to “direct screening in parents.” To be clear, Lynch did not advocate culling. However, he does ask us to entertain the idea, without specifically discussing the ethical minefield and horrifying history surrounding medical procedures without a net benefit to the recipient. For type 2 mutations, Lynch suggests that the extent to which we thwart selection is the extent to which “bad genes” will become prevalent and eventually exact their cost.

Some points in the article are argued poorly. On page 871, Lynch promises to back up the worrisome claim that our mutation rate is destined to increase, saying “...the possibility that the baseline human mutation rate will elevate over time (for reasons discussed below) motivates a strong argument...” yet he never delivers. Presumably “below” refers to the paragraph spanning the two columns of page 872, in which it is claimed that “hundreds of genetic loci influence the mutation rate either directly or indirectly,” without any citation. The paragraph ends with the statement: “It is therefore plausible that the human mutation rate is destined to slowly increase toward exceptional levels.” Despite Lynch’s additional promise early in the article (page 869) that “many of the issues addressed below were raised by Crow prior to the genomics revolution and can now be evaluated in a more

quantitative way” (see Crow 1997, 2000), there is no calculation here, only an undocumented claim of plausibility.

In arguably the best-supported calculation in the article (page 872, right-hand column), Lynch predicts that, if selection were completely relaxed, the fitness of the human population will decrease at a rate of 1% per generation, due to mutations throughout the genome. However, in his attempt to bridge his demonstration of the effectiveness of culling and this calculation of a 1% decline in fitness, on page 872 Lynch states: “For the most extreme case of completely relaxed selection ($s_n = 0$), beneficial alleles will ultimately be lost entirely ($\hat{p}_n = 1.0$).” This statement is true only for unidirectional mutation, but Lynch’s next sentence makes it clear that he is referring to mutations among the four nucleotides (also called “base-substitution mutations” earlier in the article). What will actually happen in this case, if selection is absent, is that there will be an equilibrium in which the four nucleotides are present in frequencies determined by the relative rates of mutation among them. This may seem like a minor mistake, but arguments about eugenics should be free from both technical and fundamental error. More fundamentally, there are many reasons to doubt the modeling assumption that selection has been relaxed.

Most surprising was Lynch’s failure to consider the environment in which fitness should be measured, or to consider that the fitness that matters most to humanity is fitness in present and future environments. Lynch lists “removal of visual acuity issues by optometry” as a medical intervention that may eventually reduce the fitness of humanity. But as Crow put it, “Who worries about having to wear spectacles?” (Crow 2000). While myopia may have had an important fitness cost in Paleolithic times, glasses are now widely available and seem likely to remain so. Of course for other disease traits, increased prevalence might come at greater cost. However, many medical interventions may become less costly over the time frame of decades to centuries that Lynch considers.

As our knowledge of human genetics continues to grow, mutations will shift from the undetectable type 2 category to become actionable type 1 mutations. Already, several alleles associated with refractive error and myopia have been identified (Verhoeven *et al.* 2013). Does this place near-sightedness alleles within the type I category for which we are asked to contemplate culling?

Lynch fails to consider that humanity may be selected for *increased* fitness in current and future environments. Although he worries about medical technology that reduces selection, he fails to consider selective impacts of other technologies. For example, selection may be acting on our ability to cross busy streets, to avoid drinking and texting while driving, and to avoid firearms. Accidental injury, suicide, and homicide are respectively the 1st, 2nd, and 5th most common causes of death in the United States for people aged 1–44; together they are more common than cancer, heart and liver disease, stroke, diabetes, and asthma put together (Centers for Disease Control and Prevention 2016).

Lynch states that we thwart selection when we reduce variation in the number of children per family, and that we will see increasing costs of this unless we alter our course. He mentions “the two-child syndrome in middle-class neighborhoods in westernized societies,” but cites no evidence that coefficients of variation in the number of children per parent have actually fallen. In fact, the fraction of women aged 40–44 in the United States who are childless rose from 10% in 1976 to 18% in 2008 (Livingston and Cohn 2010). Thus, it appears that the number of children remains highly variable and selection may still be effective, even in a westernized society.

Indeed, by focusing on human genetic issues that are particularly worrisome for technologically advanced nations, Lynch may be perceived as pitting the residents of such nations against the rest of humanity. Such ambiguity fosters misinterpretation. Moreover, Lynch fails to consider that selective effects within developed nations may have a very limited impact on humanity in general, given that westernized countries are genetically intertwined with the human majority.

Even given the unlikely scenario that the combination of modern medicine and family planning were to prevent selection postpartum, it is estimated that 30–40% of all conceptions result in miscarriage, of which at least 50% are attributed to genetic abnormalities (Hurt *et al.* 2012). This argues strongly against the suggestion that humans will soon escape the effects of genetic selection.

We also disagree with Lynch’s assertion of human exceptionalism and statement of “the uniquely human goal of intentionally ameliorating the effects of mutation.” Lynch does not make the case that the goal to survive and reproduce via modern medicine is fundamentally different from the goal of individuals in other species to survive and reproduce no matter the genetic “hand” that each has been dealt.

Lynch recommends we gather more information, calling for the “establishment of stable, standardized, multigenerational measurement procedures for various human traits.” This could be a good thing. However, given the history of eugenics, a call to gather information about the genetic health of our species that is uncoupled from the goal of improving medical care for individual patients may be viewed with suspicion.

Lynch concludes with a speculative and alarming discussion in which he says we have reason to be particularly concerned about the deterioration of our mental capacity. With his plea: “What will it take to promote serious discourse on the slowly emerging, long-term negative consequences of policies jointly promoted by political, social, and religious factors?” Lynch appears to lament that a predicted 1% fitness decline per generation does not provide enough motivation to alter our course. He goes on to state that “...there is no obvious technological fix for the uniquely human goal of intentionally ameliorating the effects of mutation, nor is there a simple ethical imperative for doing otherwise, short of refocusing our ethical goals on future descendants.” We understand this to mean that, despite the current lack of tools and the absence of an agreed-upon ethical mandate, we must change our ethical values and take the accumulation

of deleterious mutations seriously enough to do something about it.

The burden of proof was wholly on Lynch to support his thesis that contemporary medicine, family planning, and other modern practices are likely to dangerously reduce the fitness of the human population. Lynch failed to meet this burden of proof on multiple points. Lynch holds that his conclusions are similar to those which others had arrived at previously. Indeed, nearly every point Lynch makes, including his concern about increases in the mutation rate and his call to focus on mental capacity, can be found in the article he cites by Muller (1950). Both Muller (1950) and Crow (1997) hold important ideas worth reading. However, reiterating their concerns without the important caveats they discuss seems reckless. In some times and places, an agreed-upon mandate to pursue eugenics has been present, with disastrous outcomes.

We urge *GENETICS* to establish clear policies requiring that any article touching on human eugenics—*e.g.*, one that entertains strategies to alter human allele frequencies through procedures that do not clearly benefit the recipients—do so with the highest level of rigor, sensitivity, humility, ethical perspective, and historical context. Otherwise, eugenics is a chapter best left closed.

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