Genetic Justice Must Track Genetic Complexity

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> *To alleviate this current suffering and to help prevent many future victims of genetic injustice from being created, we need to find and study the genes that give rise to these diseases. Once we have found the genetic culprits, we can rationally search for pharmaceutical cures as well as try to develop curative genetic therapies.*
>
> James Watson, *A Passion for DNA: Genes, Genomes and Society*[1]

Many different factors influence our health prospects. The food we consume, the lifestyle we live (e.g., sedentary or active), our economic prospects, our love prospects, our gender, our age, and our education all influence our expected lifetime acquisition of what John Rawls calls the "natural primary goods" (e.g., health, vigor, imagination, and intelligence).[2] Our well-being is also influenced by the natural endowments we inherit from our parents. All people have two copies of most genes, one from their mother and one from their father. Genes are the fundamental physical and functional unit of heredity; they "specify the proteins that form the units of which homoeostatic devices are composed."[3]

The prospect of human genetic interventions, like gene therapy, raises our hopes that one day we may be able to combat more effectively the often tragic consequences of the natural lottery of life. There are currently 833 approved gene-therapy trials in America and 358 in Europe.[4] The approval of the first commercial gene therapy product was recently reported in the journal *Human Gene Therapy* (September 2005). In an editorial of that issue of the journal James Wilson, the Editor-in-Chief, reported that Gendicine, a biological agent that treats patients with head and neck cancer, was being distributed by the Chinese company Shenzhen SiBiono GeneTech (Shenzhen, China). "As of July 31, 2005, Gendicine has been used to treat more than 2600 patients, with a projected 50,000 patients to receive this product by 2006."[5]

New genetic technologies could have an important impact on human health, longevity, and even intelligence, and thus we must take seriously the question of what constitutes a just regulation of such technologies. What will the demands of distributive justice be in the postgenetic revolutionary society? A society that possesses the ability to directly intervene in the natural lottery of life through somatic (or even germline) therapies and enhancements, as well as preimplantation genetic diagnosis (PGD). What values and principles should

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inform the regulation of these new genetic technologies? To adequately answer these questions we need an account of *genetic justice*, that is, an account of what constitutes a fair distribution of genetic endowments that influence our expected lifetime acquisition of natural primary goods (health and vigor, intelligence, and imagination). These are goods that every rational person has an interest in. The decisions we now make regarding the regulation of human genetic technologies will determine how quickly and effectively these benefits are brought into existence, as well as who receives these benefits.

Philosophers posit theories of distributive justice that strive to help us deliberate about what would constitute a "fair distribution" of the various benefits and burdens of social cooperation. Some believe that we can give specific conclusions to the questions raised by genetic justice[6] whereas others caution against making such judgments on the grounds that we are currently ill equipped to make such judgments.[7] In this paper I argue that a necessary condition of a defensible account of genetic justice is that it must track *genetic complexity*. Genetic complexity encompasses phenomena such as polygenetic traits, gene–gene interactions, and complex environmental influences.[8] By tracking genetic complexity, the principles of genetic justice will (at least for the foreseeable future) be largely indeterminate. Such indeterminacies should not be regarded as a failure to utilize or properly execute the skills of analytic philosophy. Rather, such indeterminacy simply reflects the realities of the complex nature of both human genetics and the demands of justice in the real, nonideal world, that is, a world that is characterized by both scarcity and pervasive disadvantage.

More specifically, I argue that *pluralistic prioritarianism* is a theoretical position well suited for tracking genetic complexity. Prioritarians maintain that benefiting people matters more the worse off these people are.[9] But a defensible version of prioritarian justice needs to be pluralistic in the following two ways. First, it must recognize that diverse forms of disadvantage pervade our societies (e.g., genetic disease, poverty, crime, accidents, etc.) and there are a plurality of ways of mitigating disadvantage. The collective effort to mitigate these diverse disadvantages will come from the same inevitably limited budgets. Second, prioritarians must be pluralistic in that they seek to balance their prioritarian commitments with other *values*, such as utility and freedom. Consideration must be given to the severity and pervasiveness of different forms of disadvantage, the costs of mitigating these different disadvantages, and the likelihood that the benefits of mitigation will be realized.

The Impact of the Genetic Lottery of Life

Genetic inequalities permeate our societies. These inequalities are not quantitative inequalities; rather they are *qualitative* inequalities. Justice is concerned with both kinds of inequalities. Economic inequalities are the most common form of quantitative inequalities. People can have differing amounts of wealth and income. But this does not exhaust the scope on inequalities justice seeks to address. Inequalities in opportunities for education, for example, are typically qualitative inequalities rather than quantitative ones. Children may receive the same number of hours of instruction but the quality of instruction they receive could be very unequal. Similarly, although all citizens have

approximately the same quantity of genes (estimates suggest there are between 20,000 and 25,000 protein-coding genes), the quality of our genetic constitutions can vary significantly.

Unlike socioeconomic inequalities, which are a mix of both brute luck factors (e.g., natural endowments, social position, etc.) and choice (e.g., consumption habits, attitudes toward saving and work, etc.), genetic inequalities are *100%* brute luck. We inherit our genetic endowments from our parents, and they inherit theirs from their parents, and so forth. No individual is responsible for the genetic endowments he or she is born with. Furthermore, the life prospects for the least advantaged in the "genetic lottery" of life are often extremely grim. Consider, for example, that in America the average life expectancy is around 77 years of age. That number will vary depending on factors like gender, race, and wealth. Although these factors influence the life prospects of Americans, none of them come close to the extent to which *genetic variations* impact the life expectancy of the worst endowed.[10] Americans born with average genetic constitutions can expect much greater life prospects for things like health, longevity, and intelligence than those born with the worst genes. Children born with infantile Tay-Sachs will die by five years of age. People born with a mutation of the FMR1 gene will develop Fragile X Syndrome, the symptoms of which can vary from slight learning disabilities to mental impairment. No one deserves the genes they are born with. The results of the "genetic lottery" are arbitrary, and they are often tragic, both for the victims themselves and their loved ones and families.

The prevalence of the worst genetic disorders, like infantile Tay-Sachs, is extremely small. But there are over 6000 known single-gene disorders, which occur in 1 out of every 200 births.[11] "A single-gene disease is a disease caused by a single malfunctioning allele. Such diseases typically can develop in practically all usual environments."[12]

The most prevalent diseases—like heart disease, cancer, and diabetes—are not caused by a single malfunctioning allele. These more common diseases are *multifactorial* diseases. Their development depends on a variety of factors beyond our genetic constitutions. Environmental factors like diet and lifestyle (e.g., exercise, smoking, stress levels, etc.) often play a more important role in determining our risk of developing multifactorial diseases. The American Heart Association estimates that, in the year 2001, 64,400,000 Americans had one or more forms of cardiovascular disease. Cardiovascular diseases are responsible for 1 out of every 2.6 deaths. Coronary heart disease caused 502,189 deaths in 2001 and is the single leading cause of death in America today.[13] This is followed closely by cancer. Taken together, heart diseases and cancer account for over half of all deaths in America. Our genes do play a role in our susceptibility to multifactorial genetic disorders. For instance, inheriting faulty BRCA genes gives women a greater risk of developing breast cancer. But for many debilitating conditions, environmental factors play a much greater role in our susceptibility to disadvantage.

What will the demands of distributive justice be in the postgenetic revolutionary society? Where do the current and possible future benefits of biomedical research figure in an account of justice? These are questions we must begin to grapple with if we hope to institute a just regulation of new genetic technologies. But we must ensure that our desire to mitigate genetic disadvan-

tage is tempered by an appreciation of the fact of genetic complexity as well as a recognition of the other demands of justice (e.g., the duty to mitigate other forms of disadvantage, respect for reproductive freedom, etc.).

Tracking Genetic Complexity

Informed engagement with the topic of genetic justice promises to help narrow the gap between the related disciplines of political philosophy and bioethics and will, I hope, shift philosophical debates from analyses that function at the level of *ideal theory* to those that take seriously the constraints of nonideal theory (or the realities of the real world).[14] Nonideal theorists maintain that a philosophical examination of political values should be appropriately *fact sensitive*. To achieve fact sensitivity, a theory of justice must be cognizant of a range of facts that constrain or complicate the challenges of mitigating various forms of disadvantage. Such considerations may include the facts of scarcity, noncompliance, indeterminacy, human vulnerability, and fallibility. One important consideration that an account of genetic justice must consider is genetic complexity.

To take genetic complexity seriously, justice theorists ought to embrace pluralistic prioritarianism. Prioritarians maintain that it is morally more important to benefit the people who are worse off. But a defensible version of prioritarianism needs to be pluralistic in two ways. First, it must recognize that diverse forms of disadvantage pervade our societies (e.g., genetic disease, poverty, crime, accidents, etc.). These different forms of disadvantage give rise to a plurality of possible ways of mitigating disadvantage. It is imperative that an account of genetic justice recognize these considerations. Many genetic disadvantages, for example, can be mitigated without recourse to actual genetic manipulation. For example, those whose genetic constitutions put them at a higher risk for suffering disadvantage may be able to avoid the actual disadvantage through environmental interventions (e.g., diet, exercise, etc.)[15] or medical interventions that do not alter one's genetic constitution (e.g., pharmacogenetics). So the distribution of socioeconomic goods, or nongenetic intervening medical provisions, will have a large impact on the natural primary goods of even the "genetically disadvantaged."

Determining what prioritarian prescriptions require in terms of remedying genetic disadvantage really depends on who we include in the category of the genetically disadvantaged. To limit this category of people to those with single-gene disorders that cannot be mitigated through environmental intervention would be to identify a very small portion of the population. Furthermore, some of these people will not fare the worst in terms of their expected lifetime acquisition of natural primary goods. Those born with single-gene disorders can have very different life prospects, as the severity and onset of these diseases can vary greatly. Children born with infantile Tay-Sachs Disease, for example, will lose or fail to gain motor and mental skills. This is followed by paralysis and death by the age of 5. Their condition can be contrasted with the life prospects of those who suffer from a late-onset single-gene disorder like Huntington's Disease. Onset of Huntington's Disease usually occurs in the fourth decade. The prognosis for the disease is progressive disability, with death occurring 10–12 years from the onset of the symptoms.[16] So the expected

lifetime acquisition of natural primary goods for individuals born with one of the 6000 known single-gene disorders can vary drastically.

If we expand the category of the genetically disadvantaged to include those individuals whose genetic constitutions make them more susceptible to prevalent multifactorial disorders (e.g., cancer), then the members of this group will constitute a much more sizable portion of the population. Furthermore, this would also complicate the story of what form of intervention (e.g., gene therapy, education about the dangers of obesity or smoking, early screening, socioeconomic justice, etc.) will best promote the expected lifetime acquisition of natural primary goods for the genetically disadvantaged. These kinds of considerations will impact the priority a theory of genetic justice ought to place on the availability of genetic interventions that seek to directly redress the negative consequences of genetic disadvantage.

One strategy for addressing these types of concerns is to define the category of the genetically "least advantaged" as those individuals whose genetic constitutions place them below half of the median for the expected lifetime acquisition of natural primary goods.[17] An attractive feature of this strategy of identifying the most pressing forms of genetic disadvantage is that it does not necessarily define membership in this group by the type of genetic disease one has (e.g., single-gene disorder vs. multifactorial). The relevant considerations are the onset and severity of one's genetic disadvantage. Furthermore, by defining genetic disadvantage in this way we recognize that genetic disadvantage can vary with environment. For example, Sickle Cell Disease is common in many parts of the world where mosquito-borne malaria is present. Sickle Cell Disease is the most common single-gene disorder in African-Americans, affecting 1 in every 375. Globally, a quarter of a million children are born with the disease every year, mainly in Africa, the Mediterranean, and Arabia and Asia.[18]

In addition to recognizing the different forms of disadvantage that can impact our well-being, as well as the different possible measures for redressing genetic disadvantage, prioritarians must also be pluralistic in that they seek to balance their prioritarian commitments with other values (e.g., such as utility and freedom). Consideration must be given to the severity and pervasiveness of different forms of disadvantage, the costs of mitigating these different disadvantages, and the likelihood that the benefits of mitigation will be realized. Such considerations require a thorough engagement with the fact of genetic complexity. Diseases can vary drastically in terms of their *prevalence*, their *age of onset*, and the *severity of their disadvantage* (e.g., death, mental retardation, physical impairment, etc.). All of these factors must be taken into consideration if an account of genetic justice is to give due consideration not only to redressing genetic disadvantage, but also to the more general demands of societal fairness (e.g., redressing socioeconomic disadvantage or healthcare needs that have nothing to do with genetic intervention).

Prioritarians would not have to be pluralistic prioritarians if, for example, the following hypothetical scenario was an accurate depiction of genetic disadvantage in the real world:

> *Hypothetical scenario:* All disadvantage in the world stemmed from our susceptibility to equally common early-onset single-gene disorders of equal severity. Furthermore, the disadvantages of genetic disease could

> be prevented or cured through noninvasive, risk-free, costless genetic therapies.

If the scenario of the postrevolutionary world were like this hypothetical scenario, then it would be much easier to determine what the prescriptions of genetic justice are. This would be the case because in this hypothetical scenario considerations of utility *perfectly cohere* with those of priority. If those most in need are also those we can help with minimal cost for maximum benefit, then a very stringent presumption in favor of directly mitigating genetic disadvantage via genetic intervention would exist. In such a scenario one might believe that justice requires that we implement a genetic decent minimum. But the case for such a principle is complicated by the fact that many diseases are very rare; genetic disorders can also vary in terms of when the symptoms are manifest in a patient and how severe the disadvantage is. Such complexities can arise even in the case of single-gene disorders.

> The complexity in both Huntington and fragile X diseases arises from a segment of the gene called a triplet repeat. A triplet repeat consists of repetitions of a sequence of three bases. In recent years, researchers have discovered that the number of repetitions affects the age of onset of these diseases, the severity of the symptoms, and even whether the disease will appear at all. However, although the gene is inherited from the parents, the precise number of repeats is not inherited. In some cases, the number of repeats will increase from one generation to the next. In the case of fragile X, the degree of increase also depends on the sex of the parent. As a result of this type of complexity, a person in a family with a history of one of these triplet-repeat diseases may be healthy but have a child affected by the disease.[19]

Furthermore, directly mitigating genetic disadvantage through something like genetic therapy would be very costly (at least for the foreseeable future), and it would also be a procedure that carries risks for those involved. In the case of *somatic* genetic therapy, the risk would fall solely on the patient. If the intervention is a *prenatal* genetic therapy, there would likely be a risk to the mother and the fetus. And in the case of *germline* interventions, there might also be a risk to future generations.

The cost of directly mitigating genetic disadvantage through genetic intervention is something we need to bear in mind given the nonideal facts of pervasive disadvantage and scarcity. Many of those who are worse off in terms of their expected lifetime acquisition of natural primary goods are worse off, not because of their genetic endowments, but because they lack access to adequate housing, basic healthcare, or long-term economic security. So the distribution of *socioeconomic* goods also has a dramatic impact on the health and well-being of a population. Concerns of genetic justice must be balanced against such considerations. In light of these considerations, and those raised by the fact of genetic complexity, prioritarians should reject the principle of a genetic decent minimum and advocate a distributive principle that accounts for the indeterminacies of genetic complexity.

Elsewhere I have argued in favor of a principle I call the "lax genetic difference principle,"[20] a principle that takes seriously the indeterminacies of

genetic complexity. This principle states that genetic inequalities (important to the natural primary goods) are to be arranged so that they are to the greatest *reasonable* benefit of the least advantaged. Critics might charge that the insertion of a "reasonableness" clause is problematic because it leaves the prescriptions of genetic justice largely indeterminate. But the fact that the prescriptions of genetic justice are, at least for now, indeterminate is not evidence of a failure to fully utilize the analytic tools of philosophy. Rather, such indeterminacy is evidence that we have taken the fact of genetic complexity seriously. Any serious account of genetic justice must track genetic complexity. We should not treat the duty to remedy genetic disadvantage as if it were separate from the more general obligation to mitigate disadvantage. By integrating an account of genetic justice into a pluralistic prioritarian conception of justice, philosophers should be better positioned to develop an ethical framework that can help us secure fair terms of social cooperation in the postgenetic revolutionary era.

Conclusion

Many contemporary debates about distributive justice function almost exclusively on the distribution of what John Rawls calls "social primary goods" (e.g., rights, income, self-respect), whereas accounts of just healthcare tend to focus almost exclusively on access to healthcare. The former ignore (or are ill equipped to deal with) the issue of just healthcare, and the latter tend to ignore the more general issue of societal fairness. In "Broadening the Bioethics Agenda" Daniel Brock addresses these kinds of concerns, especially those facing accounts of just healthcare. He highlights two shortcomings of the bioethical discussions of justice or equity: First, that "the focus on establishing a right to health care has left bioethicists largely silent on the important and complex moral issues faced when limited health care resources must be prioritized."[21] And, second, that the focus on inequalities in access to healthcare has ignored the great impact social determinants play on our life prospects.

Parallel shortcomings exist in contemporary debates about distribution justice more generally. Many "rights-based" theories of justice adopt a *cost-blind* approach to rights protection and are thus ill equipped to address the issue of trade-offs in rights enforcement that inevitably arise given the fact of scarcity.[22] Furthermore, justice theorists like John Rawls often invoke a number of simplifying assumptions that bracket or ignore real-world constraints when determining what the demands of justice are. In *A Theory of Justice*, for example, Rawls does this when he derives his two principles of justice under the idealizing assumptions that society is a *closed system* and a society of *normal*, *fully cooperating* members.[23]

The cost-blind approach to rights, and to the demands of justice more generally, is evident in both Rawls' defence of his serially ordered principles of justice that govern socioeconomic goods,[24] and Buchanan et al.'s invocation of the principle of a genetic decent minimum. The topic of genetic justice is perhaps the ideal topic for bridging the gap between the fields of inquiry pursued by political philosophers and those pursued by bioethicists. It is also the ideal topic for transcending the ideal theorizing rampant in both disciplines. To adequately address genetic justice, one must consider not only the impact our genetic endowments have on our expected lifetime acquisition of

natural primary goods, but also the impact of nongenetic intervening medical provisions as well as social determinants.

To link the two related disciplines of political philosophy and bioethics, one must be cognizant of the different aims such theorizing can have. These differences are addressed by Søren Holm in a recent editorial in the *Journal of Medical Ethics*. Holm argues:

> The standard [bioethics] model, and to an even greater extent the rhetoric of ethics, often imply that there is only one right solution to each policy making decision, and that it is possible to find this solution, and to know that it is the right decision. . . . In contrast, theorizing about deliberative democracy proceeds from the assumption that whereas there might be a right solution, it is often impossible to find this solution or to know that it is the right solution in any absolute sense. The best we can do is to outline the area of acceptable policies, and then choose a policy within this area through a deliberative, democratic process.[25]

The argument I have advanced in this paper is not one that seeks to win a philosophical argument. Rather, my aim was to help us *deliberate* about legitimate public policy in a morally pluralistic liberal democracy. Such an enterprise will, by its very nature, end up somewhat indeterminate, as Holm notes. I have not advanced concrete policy prescriptions concerning, for example, access to genetic therapies. Rather, I believe that accounts of genetic justice that take genetic complexity seriously will help lead us to a certain range of regulations (e.g., ones that promote innovation and recognize the different dimensions of human disadvantage) rather than a different range of options (e.g., ones that presuppose genetic determinism or ignore the expected harm of existing genetic inequalities). Furthermore, a pluralistic prioritarian account of genetic justice will help us to make explicit the *reasons* why we should consider a certain range of policy prescriptions rather than a different range of policies. But I have not sought to preempt the public debate on these important and contentious topics. I believe the philosopher has an important role to play, but a political philosopher who seeks to engage, in a substantive manner, with issues of public policy should be aware of the limitations of a philosophical analysis of political values. We can better ensure that our theorizing about genetic justice does not transcend these limitations by invoking an account of genetic justice that tracks genetic complexity.

Notes

1. Watson J. *A Passion for DNA: Genes, Genomes and Society*. Oxford: Oxford University Press; 2000:169.
2. Rawls J. *A Theory of Justice*. Cambridge, Mass.: Harvard University Press; 1971.
3. Childs B. *Genetic Medicine: A Logic of Disease*. Baltimore, Md.: Johns Hopkins University Press; 2003.
4. Taken from *Journal of Gene Medicine* clinical trial site. Available from: URL: http://www.wiley.co.uk/genmed/clinical/.
5. Wilson J. Editorial. *Human Gene Therapy* 2005;16:1014.
6. Buchanan A, Brock D, Daniels N, Wikler D. *From Chance to Choice: Genetics and Justice*. Cambridge: Cambridge University Press; 2000:101. The authors argue that two central conclu-

sions should guide public policy choices in the age of genetic intervention. The first is that there is a principled presumption that genetic intervention to prevent or ameliorate serious limitations due to disease is a requirement of justice. And, second, that justice may require regulating conditions of access to genetic enhancements to prevent exacerbations of existing unjust inequalities.

7. Lindsay R. Enhancements and justice: Problems in determining the requirements of justice in the genetically transformed society. *Kennedy Institute of Ethics Journal* 2005;15(1):3–38 at p. 5.
8. Alper J. Genetic complexity in human disease and behaviour. In Alper J, Ard C, Asch A, Beckwith J, Conrad P, Geller L. *The Double-Edged Helix: Social Implications of Genetics in a Diverse Society*. Baltimore, Md.: The Johns Hopkins University Press; 2002:22.
9. Parfit D. Equality or priority? In: Clayton M, Williams A, eds. *The Ideal of Equality*. Basingstoke, UK: Palgrave, Macmillan; 2000:101.
10. However, race and gender do influence our susceptibility to certain genetic diseases. For example, African Americans are more susceptible to Sickle Cell Disease. It affects approximately 1 in every 375 African Americans. Tay-Sachs Disease is most prevalent among Jews of Eastern European descent and French-Canadians and Cajuns in Louisiana. The incidence rate of Fragile X Syndrome is much higher in boys (1 in 2000) than in girls, and the effects are typically milder for girls.
11. Genetic Disease Information—Pronto! Available from: URL: http://www.ornl.gov/sci/techresources/Human_Genome/medicine/assist.shtml.
12. See note 8, Alper 2002:20.
13. See American Heart Association home page. Available from: URL: http://www.americanheart.org/.
14. The distinction between ideal and nonideal theory is not given rigorous classification in the existing literature. As Andrew Mason (Just constraints. *British Journal of Political Science* 2004;34:251–68 at 265) notes, this distinction is employed by John Rawls in *The Law of Peoples*. An account of justice in ideal theory must recognize "some moderately strong feasibility constraints which require it to be realistic in the best of foreseeable conditions" (Mason, 2004:265). Rawls describes ideal theory as being *realistically utopian*. Political philosophy is realistically utopian "when it extends what are ordinarily thought of as limits of practical political possibility" (Rawls, *The Law of Peoples*. Cambridge, Mass.: Harvard University Press; 1999:6). This contrasts with nonideal theory, which is concerned with problems of noncompliance or unfavorable (historical, social, or economic) conditions. Nonideal theory is much more *fact-sensitive* than ideal theory.
15. Environmental interventions can even be pursued in the case of some single-gene disorders. The mental retardation caused by phenylketonuria (PKU), for example, can be prevented if the patient consumes a low-protein diet.
16. Connor JM, Ferguson-Smith MA. *Essential Medical Genetics*. Oxford: Blackwell Scientific Publications; 1984:190.
17. The genetically least advantaged are a *subset* of the more general category of individuals who are least advantaged in terms of their expected lifetime acquisition of natural primary goods. Other members of this category include those in serious accidents and those who fare poorly in terms of the acquisition of social primary goods (e.g., the malnourished).
18. Sickle Cell Disease. Available from: URL: http://www.ygyh.org/sickle/whatisit.htm.
19. See note 8, Alper 2002:25–6.
20. Farrelly C. The genetic difference principle. *American Journal of Bioethics* 2004;4(2):W21–8.
21. Brock D. Broadening the bioethics agenda. *Kennedy Institute of Ethics Journal* 2000;10:21–38.
22. See Holmes S, Sunstein C. *The Costs of Rights: Why Liberty Depends on Taxes*. New York: W.W. Norton & Company; 1999, for a compelling argument against the cost-blind approach to rights.
23. Supporters of Rawls have attempted to rectify some of these shortcomings by adding healthcare to the list of things governed by the principle of fair equality of opportunity. See Daniels, N. *Just Health Care*. Cambridge: Cambridge University Press; 1985.
24. See my book *Justice, Democracy and Reasonable Agreement*, chapters 1 and 2. Basingstoke, UK: Palgrave MacMillan; 2007.
25. See Holm S. Bioethics down under—Medical ethics engages with political philosophy. *Journal of Medical Ethics* 2005;31(1):1.