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Direct-to-consumer genomics on the scales of autonomy

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ABSTRACT

Direct-to-consumer (DTC) genetic services have generated enormous controversy from their first emergence. A dramatic recent manifestation of this is the Food and Drug Administration's (FDA) cease and desist order against 23andMe, the leading provider in the market. Critics have argued for the restrictive regulation of such services, and even their prohibition, on the grounds of the harm they pose to consumers. Their advocates, by contrast, defend them as a means of enhancing the autonomy of those same consumers. Autonomy emerges as a key battle-field in this debate, because many of the 'harm' arguments can be interpreted as identifying threats to autonomy. This paper assesses whether DTC genomic services are a threat to, or instead, an enhancement of, personal autonomy. It deploys Joseph Raz's account of personal autonomy, with its emphasis on choice from a range of valuable options. It then seeks to counter claims that DTC genomics threatens autonomy because it involves manipulation in contravention of consumers' independence or because it does not generate valuable options which can be meaningfully engaged with by consumers. It is stressed that the value of the options generated by DTC genomics should not be judged exclusively from the perspective of medical actionability, but should take into consideration plural utilities. Finally, the paper ends by broaching policy recommendations, suggesting that there is a strong autonomy-based argument for permitting DTC genomic services, and that the key question is the nature of the regulatory conditions under which they should be permitted. The discussion of autonomy in this paper helps illuminate some of these conditions.

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INTRODUCTION

In November 2013, the US Food and Drug Administration (FDA) created shock-waves around the world by issuing a cease and desist order against 23andMe, the dominant provider of direct-to-consumer (DTC) genomic services.[1] 23andMe, in common with several other companies worldwide, offered genetic testing services directly to consumers via online platforms, without physician involvement and at increasingly reduced prices. The FDA's move was a dramatic culmination of heated controversies that such services had provoked among clinicians, bioethicists, regulators and ordinary citizens. The FDA gave two main reasons for its order. First, the company's failure to comply with the agency's requirements for authorisation, regarding which it had applied and entered into negotiations with the FDA. Second, the harm its activities posed to consumers of 23andMe's services. Of course, the FDA's order needs to be understood and evaluated in the specific context of the US health regulatory framework and the course of conduct on which 23andMe had embarked. But, as the excited flurry of commentary in the media and blogosphere illustrated, the second reason offered by the FDA resonated more broadly among those concerned with DTC genomics. Indeed, concerns about the potential harmfulness of DTC genomic services had been repeatedly voiced by regulatory and other expert bodies, both in the USA and Europe, for some time prior to the FDA's momentous decision.[2 3] These harms include risks of inappropriate dosage adjustment, decisions to undergo unwarranted diagnostic procedures, the creation of needless anxiety or false reassurance, and the invasion of consumer's privacy. In addition to these harms to consumers, other concerns included the danger of ill-founded requests for diagnostic services from such consumers overburdening the healthcare system and unnecessarily depleting scarce healthcare resources.

In 2010, the FDA had already foreshadowed its concerns about the risk of harm entailed by DTC genomics in letters to several DTC genomics providers.[4] In a similar vein, a number of professional medical societies had issued policy recommendations spelling out serious concerns about DTC genomics, in particular, reservations about their analytic validity and clinical utility, and advising consumers to refrain from undergoing such tests. In light of such concerns, many critics have called for the strict regulation, and even the outright prohibition, of DTC genetic services.[3] Given the supposed lack of adequate supervision by a physician or genetic counsellor in the DTC genetics model, the main strands of the harm argument are twofold: (1) consumers can be misled into believing the information that they receive is sufficiently reliable to be medically actionable; (2) even if any information they receive is medically actionable, in principle, consumers may not be equipped to use that information in a way that benefits them. These risks can have various undesirable knock-on effects, such as bad decision making about diagnostic procedure or lifestyle, needless distress, inappropriate use of resources, and so on.

However, this scepticism about DTC genomic services is only one side of a highly polarised debate.[5] Proponents of such services have defended them primarily as enhancing the autonomy of their users, providing them with valuable information that empowers them to make valuable health and lifestyle decisions. Such claims can be interpreted as directly contradicting the harm-based arguments noted above, because one salient way of interpreting harm is as a threat to autonomy. This is not to

suggest that all harms that are potentially associated with DTC genomics are automatically and comprehensively translatable into autonomy harms. However, most of the supposed harms of DTC begin with the consumer deciding (for good or bad reasons) to obtain genomic information DTC and then how best to act upon it. Whether the consumer will unnecessarily burden the healthcare system (which is not per se an autonomy harm) has its roots in the concern that the consumer has been given misleading information which, in turn, signals that his autonomy has been undermined. Therefore, autonomy is central in the assessment of DTC and it is important to clarify the notion of autonomy in play, in order to determine whether DTC is a threat or, instead, a means of realising that value. For the purposes of this paper, I shall draw on the influential conception of personal autonomy elaborated by Joseph Raz in *The Morality of Freedom* as part of a broader liberal perfectionist theory of politics.

RAZIAN AUTONOMY

On the Razian interpretation, autonomy is the value that consists in becoming the 'part-author' of one's life through making a series of life-shaping choices in the course of navigating within a given social context.[6] According to Raz, autonomy is conditioned upon the presence of appropriate mental abilities, the existence of an adequate range of options and independence from others (p.372):

> If a person is to be maker or author of his own life then he must have the mental abilities to form intentions of a sufficiently complex kind, and plan their execution. These include minimum rationality, the ability to comprehend the means required to realize his goals, the mental faculties necessary to plan actions etc. For a person to enjoy an autonomous life he must actually use these faculties to choose what life to have. There must in other words be adequate options available for him to choose from. Finally his choices must be free from coercion and manipulation by other, he must be independent. All three conditions, mental abilities, adequacy of options and independence admit of degree.(p.373)

The Razian view focuses on an important dimension to autonomy by requiring the presence of an 'adequate range of options' which are 'morally acceptable'. Raz argues that the value attributed to autonomy stems at least partly from the fact that it enables individuals to choose freely from valuable options that must exhibit sufficient variety. So, for example, someone with only a multiplicity of trivial, short-term options to choose from—whether to eat now or later, whether to scratch their left or right ear—cannot realise personal autonomy in their lives. Equally, someone whose choices are driven entirely by the overriding need to avoid some imminent threat to their life may have valuable options, but will not enjoy a life of personal autonomy because the options do not exhibit the requisite variety, since they are all dominated by the life-preserving aim. It is an important implication of this conception of autonomy that we can enhance a person's autonomy by providing them with additional morally worthwhile options, but that we cannot do so by presenting them with additional worthless or morally bad options.

It is important to note that Raz's view differs from an understanding of autonomy that is common in modern bioethics. The latter focuses on an individual realising their capacity to make choices, and it requires that these choices be informed and free of coercion and undue influence. The existence of options from which to choose is assumed but not usually addressed or subjected to quality control. With all the focus being on independent choice, often it is the validity (or lack of) informed consent that becomes the sole criterion for whether autonomy is served. Critics of DTC genomics were quick to point out that DTC consumers' autonomy suffers due to the inadequate informed consent processes employed by current companies. Characteristically, the remedies to address any autonomy deficits have primarily focused on strengthening consent procedures.[7] However, the limitations of approaching autonomy exclusively via the informed consent route are well documented. As O'Neill has rightly observed:

> Informed consent procedures protect choices that are timid, conventional, and lacking in individual autonomy (variously conceived) just as much as they protect choices that are self-assertive, self-knowing, critically reflective and bursting with individual autonomy (variously conceived).[8]

Even ideal informed consent processes can, at best, ensure one dimension of autonomy, namely the existence of independent choice.

There is a broad range of conceptions of autonomy elucidating several of its dimensions, and although there is a similarly wide range of views about the value of such conceptions, it is unlikely that one dimension alone fully captures this value. Raz's conception avoids this pitfall by extending the requirements of autonomy beyond the minimum condition of self-fulfillment through independent choice. It sets stricter criteria for achieving autonomy by demanding certain qualities in the available options, and rendering such qualities integral to the value of choice. He makes a plausible case that not all kinds of options serve one's interests, and those options that fail to promote one's interests do not enhance one's autonomy. What underpins Raz's view is the notion that autonomy is key to a good life, at least in modern societies, and therefore, any setbacks to autonomy are harms to an individual. Moreover, the achievement of a good life in this account is not just an individualistic undertaking independent of social practices. By linking autonomy to the quality of options that are on offer in a certain social context, options that are socially created, defined and sustained, individual autonomy becomes a societal achievement and inseparable from the common good.

It is further worth noting that using the Razian conception enables us to formulate the autonomy-based critique of DTC in its strongest form, since much concern about DTC has precisely centred on the quality of the options it generates. It is, therefore, all the more significant if that critique can be countered on its most hospitable Razian terrain.

MANIPULATION?

In common with other understandings of autonomy, Raz's independence condition precludes others subverting one's decision making through various forms of manipulation, such as misleading advertising. One autonomy-based critique of DTC genomics involves the claim that DTC genomics companies are engaged in precisely such manipulation. On this view, companies fail to provide adequate information to consumers about the services they offer. For example, they exaggerate the potential clinical utility of such services, while also providing limited information about the research uses to which they put the data that is collected, the assignment of intellectual property rights, and the data access given to third parties.[9–14]

This objection, characteristically formulated as the failure to meet a condition of informed consent, obviously raises serious concerns. However, it can be replied that it does not identify a

problem that is either *inherent* or *unique* to the provision of DTC genomic services.[15 16] Instead, DTC genomics should comply with consumer protection legislation that is more generally applicable. Admittedly, the distinctive nature of DTC genetics, that is, the fact that it is a combination of a product (kit), laboratory test (eg, single-nucleotide polymorphism (SNP) analyses) and a service (interpretation of results relating to health but not also to other considerations, such as ancestry), poses challenges in subsuming it under existing regulatory standards.[17] However, existing regulations regarding medical devices, in vitro diagnostic tests, clinical laboratory standards, and consumer law, offer valuable starting points in fashioning a regulatory regime adapted to the distinctive nature of DTC genomic services.

Is there any reason to suppose that there is an insuperable barrier to DTC genomics companies satisfying informed consent requirements, including requirements to provide accurate information about their services? One argument centres on the fact that most DTC genomics services are provided online. This creates difficulties in verifying the identity, and competence to consent, of the individual consumer.[18] However, this objection equally applies to other services provided online, it is not specific to DTC genomics services. A more radical argument, however, is that misleading advertising is inherent to DTC genomics, because such advertising necessarily makes the false claim that it generates options that are medically actionable in valuable ways.[11] If advertisements for DTC genomics were truthful, the objection goes, they could not claim to be offering a valuable or commercially viable product.

VALUABLE OPTIONS

This radical objection feeds into the second condition on Razian autonomy. Establishing the autonomy-enhancing character of DTC genomics within a Razian framework, requires showing that it generates worthwhile options. Precisely this feature of autonomy, however, has been invoked by Cathleen Kaveny in important recent work to show that not only does DTC genomics not enhance autonomy, it may even pose a serious threat to it.[19] There are two main strands of argument in her detailed and wide-ranging critique which echo the key concerns that have already been put forward by others. The first is that the information yielded by DTC genomics does not generate valuable options because it is not medically actionable, that is, it does not generate clinical options for improving the consumer's health. The second is the claim that, even supposing that information that is in principle medically actionable is generated, its potential medical value cannot be actualised by ordinary DTC consumers. One main reason for this is the probabilistic nature of the information combined with the serious difficulties ordinary people experience when engaging in probabilistic reasoning. These difficulties may lead them to make harmful decisions, a risk exacerbated by their lack of genetic literacy. What Kaveny has done is to elaborate the commonly rehearsed arguments against DTC within the Razian framework of autonomy, thereby giving those arguments a deeper and more compelling basis.

Medically actionable information

Bearing in mind that this is a controversial area in which expert opinion divides, Kaveny and other critics are perfectly justified in raising questions about the medical actionability of the information generated by DTC genomics.[20] However, it is arguable that their skepticism is exaggerated. To begin with, the medical actionability of DTC genomics is not monolithic but rather depends on a number of key variables. One variable is the nature of the test procedure that is adopted. Most DTC genetics companies use SNP genotypes, a lower-cost technology with certain limitations. A smaller number offer whole genome or exome sequencing which generates more comprehensive data and can, in principle, lead to greater medical actionability. As sequencing becomes increasingly less expensive, it is likely to be more commonly adopted within the DTC genomics industry. Another important variable is whether what is being tested are high-penetrance genes, which have high predictive value, such as testing for BRCA1 and BRCA2 mutation (linked to breast cancer) or mutations linked to the Lynch syndrome, a serious risk factor for colon cancer.[21–23] Therefore, a blanket skepticism about the medical actionability of DTC genomics is unwarranted. This conclusion is strengthened by the fact that medical actionability is likely to increase over time, especially as more people undergo genetic testing and more data become available for analysis, which will lead to a better understanding of genetic susceptibility to disease.

Even assuming, however, that DTC generates information that is, in principle, medically actionable in a sufficient range of cases, it may be objected that consumers are typically not equipped to use this information in a way that meaningfully enhances their autonomy. A common concern is that such information is probabilistic in character, and that ordinary people typically have serious difficulties in handling probabilities without expert assistance. Genetic counselling that 'translates' the results, and places them in the context of other health data, although a well-established feature of clinical genetic testing, is mostly absent in DTC genetics. It is notable, however, that as the DTC genetics model has evolved, it has increasingly incorporated some form of counselling.[24] Nevertheless, it has not been shown that its absence seriously impairs autonomous decision making.[25–27] While evidence is not conclusive, most studies that have been conducted so far show that consumers do not suffer psychological harms, nor do they take action to alter their lifestyle in response to their genomic profiles.[28 29] Studies have also shown that there is no increase in the use of health services attributable to the consumers receiving DTC genomic data.[30]

Dealing with probabilistic data is a recurrent feature of decision making well beyond the medical context. It is hardly a problem uniquely posed by genetic information, and to present it as such smacks of genetic exceptionalism. For example, easily accessible data such as one's Body Mass Index, or blood cholesterol readings, or more complex information resulting from family history, has predictive value about one's health. Such information often has greater predictive weight than genetic information, but no argument regarding autonomy impairment has been made in this context, even if the understanding of such predictions on the part of the individual may be limited.[31] Ultimately people integrate such information into decisions they make about their lives (by acting upon it or ignoring it). If our limited abilities to process probabilistic information imperil our autonomy, surely the correct first-line response is to adopt measures to improve these abilities rather than to prohibit access to the information.[32] Such measures are not limited to, and need not necessarily involve, genetic counselling. Empirical studies examining patients' understanding of consent documents, advertising materials and so on, systematically establish ways to mitigate the 'risk of misunderstanding' through better designed information documents, aided by pictorials, web-based tools, and so on.[33]

Plural utilities

It is therefore hasty to conclude that DTC genomics fails to generate valuable medical options that can be meaningfully engaged

with by its consumers. However, a further important point needs to be made under Raz's valuable options condition. Critics have assumed that the value of the options generated by DTC genomics should be assessed exclusively from the point of view of medical actionability. Although an option of this kind is certainly desirable, enabling health improvement is only one way through which value may be acquired. There are other ways in which an option may be valuable, for example, satisfying one's curiosity, increasing one's genetic literacy, enabling participation in research and contributing thereby to science knowledge, or as a means of exploring one's ancestry. Indeed, there is increasing evidence that DTC genetics users are motivated by a variety of reasons in undergoing testing, including those described above.[34 35] Engaging with genetic testing also has an educational component insofar as individuals get a hands-on experience with genetics and its role and limitations in health and disease.[36 37] It is noteworthy that in the aftermath of the FDA's order, although 23andMe ceased offering health-related information to its users, it continued selling ancestry services and raw genetic data (without interpretation).

In short, worthwhile options generated by DTC genomics include 'personal' utilities that go beyond health improvement.[38] Of course, some of these utilities have also attracted skepticism. Is searching for one's genetics roots or traits just a form of narcissism? Is there something deeply problematic in conceiving of the 'self' as a genetic self, perhaps one detached from other important aspects of identity?[39] The answers to these questions remain open, but it is unclear why they pose a special autonomy-based problem for DTC genetics. And, even if they do pose such a problem, it may be that this cost is outweighed by other considerations. If, for example, the personal utility arising from searching for genetic relatives on a data base and comparing genomes comes at a cost, such as fostering a conception of identity in terms of genetic make-up alone, this needs to be set against potential benefits, for example, discovering the existence of half-siblings or genetic relations to parents. It can also be outweighed by the value of research participation which contributes to the common good. These personal utilities are important and have independent significance, hence they are among several considerations that need to be balanced against other benefits and costs. It is reasonable to suppose that even if in general the clinical utility of DTC genomics is low, the personal benefits generated through such services work to expand the range of valuable options, and to hence, satisfy Raz's third requirement of autonomy.

An intriguing issue concerns results that have a high predictive value for currently non-preventable or non-treatable conditions. Again, it has been argued that this information lacks value due to the absence of treatment options.[19] This argument unduly minimises the fact that people seeking this information often have salient family history, and may be living with agonising uncertainty about their own future. The option of acquiring certainty, for those who wish it, about something so important, and around which they may design life strategies, cannot lack value.[40–42] It has been further objected that if one knows enough about one's future, the life options are not those of the authentic self (the one that does not know).[43] For this argument to stand, it needs to be shown why the one with insights about the future is less authentic than the one without them. First, those who seek DTC information about such diseases are doing so because they want to receive this information (they are not forced to obtain it) and presumably this is an act of their authentic self. Their actions on the basis of this information will reflect their personalities. People are likely to react very differently to the information obtained. Some will choose to change their life plans, for example, decide not to have children, while others may choose to do so sooner than later. The variation in responses to such information may be more indicative of people maintaining their authenticity rather than losing it.

CONSEQUENCES FOR POLICY

As we saw at the outset, a recurrent concern about DTC genomics is that it poses an unacceptable risk of physical and mental harm to consumers, as well as potentially placing serious burdens on the entire healthcare system. This harm rationale has been invoked by regulatory bodies in Europe and the USA in recommending a restrictive approach to the governance of DTC genomics. This paper has dealt exclusively with the harm rationale articulated as a threat to the autonomy of consumers, that is, to the exercise of their capacity to make choices from a range of valuable options. Precisely on this autonomy-based understanding of harm, for example, critics of DTC genomics have urged a restrictive approach to the regulation of such services. Because autonomy features so prominently in the DTC debate, it is important to clarify whether it is imperilled.

In this article, I have challenged the thesis that DTC genomics is, in principle, harmful in virtue of the supposed threat it poses to autonomy. On the contrary, using a Razian framework, it is plausible to regard it as potentially enhancing autonomy. This is especially so in light of the fact that it generates valuable options, although it is important to bear in mind that the value derives from plural sources, and not exclusively from medical actionability. However, the capacity of DTC genomics to enhance autonomy depends upon its satisfaction of a number of requirements, including those governing consumer protection, for example, accurate advertisement, informed consent requirements, privacy protections, providing aids to probabilistic reasoning, the option of some form of genetic counselling and so on. Accordingly, this defence of DTC genomics in principle is not to be confused with the defence of any existing DTC genomic services, which might be deficient in various ways. The point is that these deficiencies are not inherent and ineradicable.

I have not argued that there is a positive societal obligation to provide DTC genomic services. Nor am I committed to the claim that the autonomy-based case is all-things-considered conclusive for the question of legal permissibility, though it seems to me to create a strong pro tanto case for permissibility. Autonomy is just one, albeit very important, evaluative consideration in shaping an adequate regulatory scheme. Nevertheless, it may have significant implications in its own right. For example, Raz interprets the harm principle, which licences state coercion only to prevent harm to others, in terms of threats to autonomy. If the line of argument pursued in this paper is correct, and if we subscribe to a regulatory approach based on the harm principle, then DTC genomics does not of its very nature constitute such a threat. It therefore should not be legally prohibited, contrary to what is currently the case in several countries.[44] However, if the harm principle is not the exclusive justificatory basis of regulatory constrains, my argument does not provide a conclusive case for the permissibility of DTC genomics. I have not explored this possibility here for two main reasons. First, because autonomy-based harm is likely to be a central consideration in any assessment of the legal permissibility of DTC genomics and in the regulation of biotechnology more broadly. It is therefore worth weighing DTC genomics on the scales of autonomy, even if other scales will also be needed before we answer the question of whether to allow it and under what conditions. Second, although a non-harm-based case for prohibiting DTC

cannot be ruled out, I am doubtful as to its prospects of success in light of the autonomy-based case advanced here. Appeals to the potential distress caused to DTC consumers, or to the morally inappropriate conception of personal identity supposedly fostered by DTC genomics, seem to me highly questionable bases for prohibition given the existence of an autonomy-based case for permissibility.

The aim of this article is to make progress in the controversy surrounding DTC genomics by addressing some of the underlying ethical and political questions that it raises. The verdict of autonomy, I believe, is that there is at the very least a pro tanto case in favour of the legal permissibility of DTC genomic services. The next phase in the debate requires opponents of DTC genomics either to challenge that case, or else to show that autonomy-based concerns are trumped by countervailing considerations of other kinds. If, as I am inclined to believe, the case for outright prohibition or heavy restrictions does not succeed, we should then move on to the more fertile question of the precise regulatory conditions under which DTC genomic services should be permitted. The answer to this question may legitimately vary to some extent from one jurisdiction to the other, in light of such matters as established legal doctrine and varying cultural and social conditions. But in any modern liberal society, the autonomy-based argument developed in this paper should form a central part of the framework for elaborating those conditions.

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