Karli Thompson

Professor Brutlag

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Final Paper

A Professional's Responsibility to Report Incidental Findings

Introduction

It is becoming easier and cheaper to sequence a person's entire genome. This allows for great opportunities that are saving lives. Genomics gives a researcher the opportunity to recruit a large group of people that share a disease and identify genetic variants these individuals share that might have a causal relationship to the disease. Genomics gives a doctor the opportunity to use these identified causal relationships to look for certain mutations that might be producing a patient's symptoms in order to diagnose and treat conditions rapidly. Finally, genomics gives a person of the general public the opportunity to access their genome through a DTC company and verify if they have the same gene that caused the death of a relative. Opportunities such as these represent some of the many beneficial uses for genome sequencing and genetic medicine. However, these up and coming technologies have also introduced many problems for the doctors, research scientists, and direct-to-consumer companies using them.

The Incidental Findings Dilemma

When a genome is sequenced, the results often include "incidental findings" defined as: previously undiagnosed medical or psychiatric conditions that are discovered unintentionally and are unrelated to the current medical or psychiatric condition which is being treated or for which tests are being performed. Incidental findings fall under 2

categories: anticipatable and unanticipatable. Anticipatable incidental findings are "known to be associated with a test or procedure" while unanticipatable incidental findings "could not have been anticipated given the current state of scientific knowledge" as defined by the Presidential Commission for the Study of Bioethical Issues chaired by Amy Guttman (Guttman et al. 3). The dilemma professionals are left with is what to do with these findings when they appear. Complicating this issue is differential preferences and responses of individuals to such news. How does a doctor decide whether to report an incidental finding to a patient in hopes that he will find this information useful and empowering, but at the risk of burdening a patient who will only find the same information depressing? The burden of answering this question falls on politicians. "The current challenge for public policy and professional ethics is to identify through thoughtful deliberation specific criteria that practitioners can use to determine when it is ethically permissible or obligatory for clinicians, researchers, or DTC companies to disclose and not disclose incidental findings to patients, participants, or consumers" (Guttman et al. 3).

The Presidential Commission for the Study of Bioethical Issues sought to create these criteria focusing on four ethical principles. First, respect for persons: protecting the autonomy of an individual to decide his own personal preferences and act accordingly. Second, beneficence: professionals must ensure the well-being of others and prevent imposing harm on others. Third, justice and fairness: there must be equitable treatment for all. Finally, intellectual freedom and responsibility: standards must keep in mind the importance of intellectual exploration and promote scientific progress.

The committee produced a series of recommendations that practitioners could use

as guidelines in making decisions. This is the first point on which I disagree with the present legislation on this topic. I believe that these recommendations should undergo standardization and mandatory implementation in order to protect both practitioners and patients from the problems that incidental findings create. As long as they remain optional and up to professional discretion, I believe we are allowing for differential treatment that will result in health disparities, lawsuits, and ethical burden with dramatic repercussions. In the remainder of this paper, I will go through what I feel to be the most important of these recommendations and explain why I believe this to be true.

First, the committee gave 5 overarching recommendations that can be applied to the clinical, research, and DTC company contexts. The first of these states: "Clinicians, researchers, and direct-to-consumer providers should describe to potential recipients incidental and secondary findings that are likely to arise or be sought from the tests and procedures conducted. Practitioners should inform potential recipients about their plan for disclosing and managing incidental and secondary findings, including what findings will and will not be returned" (Guttman et al. 5). I think this touches on the most important issue, what the patient is told before any genetic sequencing takes place, but it needs to be flushed out. A huge problem in healthcare today is the asymmetric information problem, when the producer and the consumer do not have access to the same information. We need to remedy this problem in genomics immediately by providing people with accurate information up-front.

The Information Problem

The first thing practitioners should inform recipients of is how often incidental findings occur. Adeline Delavande, a Professor of Economics at the University of Essex,

says that when "decisions are made under uncertainty (in this case, uncertainty of an incidental finding occurring), individuals are likely to form subjective beliefs (expectations) about the probabilities of events that are relevant to their decisions." Applied to incidental findings, individuals will guess what the probability of a practitioner discovering an incidental finding will be and decide whether they want to know what these findings are or not based on this probability. Several studies have been conducted in which researchers have looked at how accurate people's perceptions are when making various decisions. One study by Pascaline Dupas, "Do Teenagers Respond to HIV risk information? Evidence from a Field Experiment in Kenya," looked at Kenyan teenagers' perceived risk of contracting HIV from having sex with a younger partner versus an older partner. Dupas confirmed that teenage girls were underestimating the risk associated with sex with older partners and when given the accurate information, the number of sexual acts with older partners decreased by a statistically significant number. This is an example of a health related problem being aggravated by inaccurate subjective probabilities and remedied by information. I think studies need to be done on the subjective probabilities of recipients of genetic sequencing in regards to the probability of incidental findings. I believe research scientists would find that people do not have accurate perceptions and would make different decisions if they were given the correct information.

I would also mandate that practitioners give recipients a complete understanding of the actionability of the incidental findings that may result. Asymmetric information is present when people are unaware that many potentially harmful mutations are treatable and that there are actions that can be taken to improve their health or prevent it's decline

if they choose to be given the information. On the other hand, there may also be situations where recipients perceive incidental findings to be more actionable than they are and may be better off if left uninformed of such findings. If practitioners could trust that their recipients were making educated decisions about whether or not to be informed of an incidental finding, it would remove their burden to make discretionary calls that go against the individual's original choice.

On a related note, when recipients do choose to be informed of incidental findings, the idea of actionability gets complicated outside of the clinical context. In the clinical context, doctors are well informed of the actions that can be taken to treat or prevent a condition predicted by an incidental finding. However, research scientists and DTC companies are not and we must make sure that in these contexts, "disclosure of an incidental finding…does not transform a research (or producer-consumer) relationship into a clinical one" (Guttman et al. 16). Currently, research scientists and DTC companies are encouraged to make referrals to doctors that can advise their patients on action to be taken moving forward. This suggestion must be made a requirement or else this becomes not just an information problem, but also an equity problem: the second area of reform I would like to see expanded upon and flushed out.

The Equity Problem

The present legislation decided on by the committee to address the equity problem is outlined by recommendation #5: "The principle of justice and fairness requires that all individuals have access to adequate information, guidance, and support in making informed choices about what medical tests to undergo, what kind of information to seek, and what to do with information once received. The principle of justice and fairness also

requires affordable access to quality information about incidental and secondary findings, before and after testing, which when coupled with access to care can be potentially lifesaving or life enhancing" (Guttman et al. 9) While they use the language "required," there is currently no standardized list of information, guidance, and support that must be provided to recipients to ensure justice and fairness. Until these benefits are clearly defined and mandated, disparities based on socioeconomic class will persist. Accessing the information and providing guidance and support will cost practitioners extra time and money. Using the DTC context as an example, the companies providing the cheapest services will be least inclined to include these additional services with their tests because their consumers are poorer on average than the more expensive companies. They will have to charge more to include these supplementary benefits and will face the greatest risk of losing customers; so many companies will opt out of doing so. This puts their customers at the greatest risk of making an uneducated decision because they will lack access to information and to doctors that can advise them on next steps.

Now one might argue that mandating these services could make genomic sequencing too expensive for low-income populations and they may lose access to the tests themselves as a result. However, I propose the solution lies in moving DTC companies into the healthcare sector. Then, companies could bundle the test and services together in one package that insurance companies are forced to cover. This would prevent low-SES recipients from paying the information and advising costs completely out-of-pocket. I think this solution is better than the one given by the committee in recommendation 17: "Direct-to-consumer companies should aid in the creation of industry-wide best practices concerning the management of incidental and secondary

findings. These best practices should include when and how such findings will be disclosed and standards for referral to necessary clinical services. Direct-to-consumer companies should make these "best practices" publicly available to encourage broader adoption" (Guttman et al. 19). They suggest that the creation and publicizing of "best practices" will encourage companies to follow suit. I am not convinced for the reasons stated above. However, if this were the route taken to promote universal standards, I would suggest that companies be rated on set standards of quality and these ratings be provided to all potential customers. This up-front information would lower recipients' expectations for supplementary services from cheaper companies and enable them to make an educated decision when choosing a DTC company.

The Ethical Burden

Now I would like to address the specifics that need to be dealt with before thinking about implementing mandates to remedy problems like information and equity. One needed specification is an objectively drawn line that makes ethical decisions for practitioners. The possession of such life-altering information places practitioners in a very difficult spot and legislation must be passed to take ethically charged decision making off of their plate. One example of this burden is the decision to use bundled tests or discrete diagnostic tests. The advantage of bundled tests is that they are cheaper per test. The benefit of a discrete diagnostic test is that there is less chance of coming across an incidental finding. Recommendation #8 addresses the committee proposal for objectively deciding between the two: "Federal agencies and other interested parties should study the comparative benefits to patients and the cost effectiveness of using bundled tests or a battery of tests versus conducting sequential, discrete diagnostic tests"

(Guttman et al. 11). In doing a cost-benefit analysis, legislation can lift the weight from practitioners' shoulders and make decisions strictly on numbers. If the benefits of saving a practitioner and patient alike from the stress of an incidental finding outweigh the additional cost to perform more specific tests, a practitioner should be mandated to perform that form of sequencing and vice versa. In the same way, we can apply this technique more broadly by using cost-benefit analysis to draw a line (based on actionability) to determine when it is necessary to report an incidental finding and when the recipient should be kept uninformed.

One might pose the counter-argument that drawing this line compromises patient autonomy. I propose the solution to be somewhere in the middle. Cost-benefit analysis could be used to draw the line, then, recipients are informed that on one side of the line the costs have been measured to outweigh the benefits and they recommend not reporting the finding and on the other side the inverse is true. The individual may then decide if they would like to take the practitioners advice or if they would like to shift the line. They can shift it right so that more than the advised incidental findings will be reported to them. They may also shift it left so that less than the advised level of findings will be reported. I think this is a good example of a way practitioners can provide recipients with standardized, accurate information, but still respect the individual's freedom and personal preferences.

Concluding Thoughts

I believe that the solution I have just stated is the best way to ensure that the four ethical principles defined by the Presidential Commission for the Study of Bioethical Issues are achieved. Respect for persons is satisfied in that recipients are given the

autonomy to draw the line where it aligns with their personal preferences. It meets the requirement for beneficence, as practitioners will be responsible to report complete and accurate information to individuals. This guarantees that informed, educated decisions will be made based on realistic perceptions and the practitioner's responsibility to ensure well-being and prevent harm will be fulfilled. The third principle of justice and fairness is ensured by required and standardized information and follow-up procedures, so that recipients are not given differential support. Recommendations must become mandates to prevent genomics created health disparities. Finally, intellectual freedom, mainly affecting the research context, is protected when educated decision-making is promoted. If participants in research know exactly what they are signing up for, they are capable of deciding which incidental findings will be reported to maximize their own personal well-being. This allows research to progress without bearing the burden of lawsuits and ethical dilemmas.

The problem of incidental findings is a very complex and multifaceted one that cannot be entirely eliminated with guidelines like the ones I have suggested. However, I believe that legislation has a meaningful role to play in the ethical dilemmas created by genetic sequencing.

Works Cited

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