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Informed Choice in Direct-to-Consumer Genetic Testing for Alzheimer and Other Diseases: Lessons from Two Cases

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Abstract

Health-related direct-to-consumer (DTC) genetic testing has been a controversial practice. Especially problematic is predictive testing for Alzheimer disease (AD), since the disease is incurable, prevention is inconclusive, and testing does not definitively predict an individual's future disease status. In this paper, I examine two contrasting cases of subjects who learn through genetic testing that they have an elevated risk of developing AD later in life. In these cases, the subject's emotional response to the result is related to how well prepared she was for the real-life personal implications of possible test results. Analysis leads to the conclusion that when groups of health-related genetic tests are offered as packages by DTC companies, informed consumer choice is rendered impossible. Moreover, I argue, this marketing approach contravenes U.S. Federal Trade Commission policies for non-deceptive commercial communications. I conclude by suggesting ways to improve the prospects for informed consumer choice in DTC testing.

Keywords

direct-to-consumer genetic testing; APOE; informed consent

Introduction

Under the porous U.S. regulatory regime guiding direct-to-consumer (DTC) genetic testing, health-related genetic tests of varying clinical utility are available online to anyone who has enough money and saliva to be tested (Javitt and Hudson 2006). This is true despite the recommendations of a series of advisory bodies which anticipated the rise of consumer genetic testing and suggested ways to guide its growth (Parthasarathy 2007). Observers debate whether the U.S. Food and Drug Administration or other authorities can or should impose oversight of DTC genetic testing in cases where the resulting data can be seen as medical information.[1] However, this debate is clouded by a dearth of empirical information on how consumers use and react to the information they purchase from DTC companies. Further confusion arises from the widely disparate real-life implications of the specific diseases and genes at issue in DTC genetic testing. Susceptibility to a preventable disease, for example, is quite different in its practical import from susceptibility to an incurable, uniformly fatal disease. These assorted consequences are varied enough without then overlaying the uncertainties associated with specific tests, the functions of individual genes, gene-gene interactions, and lay understandings of risk (Marteau and Richards 1996,

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[1]The FDA recently deterred an American pharmacy chain, Walgreen's, from selling retail genetic test kits by questioning the legality of the kits (Pollack 2010). As medical devices, test kits are clearly under FDA oversight. However, as discussed below, testing services are more problematic.

Holtzman *et al* 1997, Wachbroit 1998, Evans, Skrzynia and Burke 2001, Lock *et al.* 2006). Nevertheless, DTC testing companies offer packages of health-related tests which include diseases from the most inconsequential to the most dire, creating intersecting planes of heterogeneity and complexity.

In an attempt to bring clarity to discussion of the implications of health-related DTC genetic testing in real life, I will focus on what is often considered one of the most worrying cases in genetic susceptibility testing, Alzheimer disease (AD). Below I will introduce two cases of susceptibility testing for AD. The lessons from these cases will lead me to explore the nature of autonomous decision-making in health-related DTC testing and to suggest that informed consent (in the consumer context, "informed choice") is a critical variable contributing to whether consumers of test products perceive benefit or harm from the disclosure of genetic information.

A Worst Case Scenario: Alzheimer Disease

Alzheimer disease is neurologically degenerative, incurable and fatal. Over a decade or more, AD progressively robs its victims of memory, life-long skill sets, and motor ability, reducing patients to a vegetative state prior to eventual death. Current treatments have only slight impact on the course of the disease. The common, late-onset form of AD (affecting people aged 65 and over) is a complex condition associated with a range of social, environmental, and genetic risk factors. Increasing age is the single most robust risk factor for AD. The risk of onset doubles every 5 years after age 65 (HHS 2009, 3). Studies of monozygotic twins have implicated both environmental and genetic factors in disease development (Gatz *et al.* 2006), and variables such as level of education, prior head trauma, and healthy lifestyle habits are often suggested as potential risk factors (HHS 2009). However no environmental factors have been proven to have direct involvement in AD pathogenesis (Bird 2008) and controlled clinical trials associating specific behaviors with specific positive outcomes in individuals are lacking (HHS 2009).

After age, the largest risk factor for late-onset AD is genetic. Dozens of genes have been implicated in AD, most having extremely weak effects. Only one gene, APOE, has emerged as an important risk factor for AD (Tsuang and Bird 2002). Each of us has two copies of the APOE gene, one from each parent, and the gene occurs naturally in one of three structural variations called ε2, ε3, and ε4. In general, people having one copy of the ε4 variant have about a three-fold lifetime incidence risk of AD compared to the general population; people with a double-dose of ε4 (two copies) have about a fifteen-fold increased risk (Ibid.). Although APOE data can be used to make statistical predictions in *populations*, it is a poor predictive tool for individuals. Approximately 42% of people who have AD do *not* have an ε4 allele (Bird 2008). Moreover, the double-ε4 genotype which most strongly predisposes people to AD is found in less than 19 percent of AD patients having a positive family history of dementia (Ibid.). Further complicating prediction, the presence of an APOE ε2 allele confers a protective effect (Farrer *et al.* 1997), and other genes which modify the effect of APOE have been identified (Seripa *et al.* 2004). Additionally, risk across different APOE genotypes differs according to sex (Farrer *et al*. 1997). And the proportion of ε4 carriers in control populations, as well as the percent of AD sufferers who are ε4 carriers, both vary according to race (Ibid.).

As Lock (2005) has correctly observed, APOE testing for prediction of AD is "no more accurate than fortune-telling" (S48). Since the disease is incurable and lacks proven prevention strategies, many experts have concluded that susceptibility testing in asymptomatic people is pointless and creates needless anxiety (e.g. ACMG 1995, ADI 1995, NIA 1996). Nevertheless, APOE susceptibility testing for AD is offered by major DTC

companies such as Navigenics and DeCode. Another well known company, 123andMe, does not offer APOE as of this writing, but has indicated that it is working towards offering the test in the future.

A major clinical study called REVEAL (Risk Evaluation and Education for Alzheimer's Disease), spearheaded by Dr. Robert Green at Boston University, has examined the impact of genetic testing of healthy first-degree relatives of people with AD and found little negative emotional impact (Roberts et al 2004).[2] However, crucially, this testing took place in a highly controlled experimental context. The test subjects received extensive pre-test information and counseling over multiple sessions, with opportunities to opt out of the study before genetic testing was done. As a result, less than half of the subjects initially enrolled (162 out of 375) continued through the entire process and received disclosure of lifetime risk for AD (Ibid.). These were carefully screened and counseled subjects, and participants received additional post-test counseling and three sets of follow-up interviews over 12 months. By contrast, consumers of DTC tests purchase bundled portfolios of genetic tests (typically not single disease testing), receive no formal pre-test counseling (not unless they seek it out), and may or may not receive any post-test counseling. Therefore, REVEAL leaves open the question of risk and benefit for consumers of DTC genetic tests.

To try to answer that question, I initiated a study of first-degree relatives of people with AD who had been tested for APOE or had "seriously considered" testing. Volunteers participated in semi-structured telephone interviews on their experience with AD and APOE testing, including perceptions, expectations, sources of information, reaction to results, etc. Unfortunately, the study was hampered by recruitment problems. Of the 20 volunteers who ultimately participated in the study, only two had undergone APOE testing. The plan to analyze and compare themes between the tested and not-tested groups was therefore confounded. However, the two individuals who were tested both turned out to have at least one copy of APOE-ε4, and both have family histories of AD. Set side-by-side as case studies, their stories offer instructive similarities and contrasts, representing genetic testing as both empowering and potentially harmful. Neither of my informants simply decided to get tested for APOE, logged onto a website, and ordered a test. The social landscape of genetic testing turns out to be more complex than that simple stereotype – a fact which itself is important to highlight. Together these accounts have implications for genetic testing as a consumer product.

"Claire"[3]

Claire is a journalist, now in her late 50s. Three decades ago, her grandmother was stricken with dementia and came to live with Claire's family. But, having finished a degree from a top tier university, Claire had already left home and was pursuing an ambitious career. "I knew something was wrong. But when you're in your 20s, you don't really think about it." Her mother quietly shouldered the burden of grandmother's care.

Many years after her grandmother's death, when Claire was in her 40s, her mother began exhibiting signs of cognitive decline. Initially Claire dismissed the problem as fatigue and the stress of running a business. But after a brief lapse in which her mother did not recognize her, Claire was jolted into action. She first brought her mother to a nearby academic medical center where the qualified diagnosis was Lewy body dementia. Seeking another opinion, Claire brought her mother to a second academic center for evaluation and was told that that the diagnosis was almost certainly Alzheimer disease. In the aftermath of the meeting, Claire

[2]See http://www.bu.edu/alzresearch/research/publications/index.html (accessed August 4, 2009).
[3]To preserve their anonymity, key features of my informants' identities have been altered.

began to recall her mother's stories about her own grandmother (Claire's great-grandmother), who had also been stricken by dementia and had died in an asylum. Still, Claire did not readily accept the diagnosis. "So my great-grandmother, my grandmother, my mother. And when I got the diagnosis from [the medical center], I thought: You know what? I don't really believe them." She sought a third opinion from another neurologist, this one almost three thousand miles away. By now, Claire's mother had deteriorated so much that she screamed for help in the airport believing Clare was abducting her. The third neurologist to see Clare's mother sent for a genetic test. Her mother had an APOE-ε3/ε4 genotype. Claire thought, "Oh *crap.* It's genetic. Oh no!"

The neurologist told Claire that she could also be tested if she was worried about heredity. After returning home, Claire decided to try it. Five consecutive physicians (some general practitioners, some neurologists) refused to order the test because she was asymptomatic. Finally, she found a naturopath who collaborated with an osteopath willing to order the test – and then Claire balked. Did she really want to know? "But I was persistent, because I thought . . . I need to know. It's in my family. Maybe I've dodged the bullet. Maybe I'm taking after my biological father instead of Mom."

The test results were mailed directly to her home. She had the same genotype as her mother. "It's like somebody is handing you a death sentence. . . . I can't tell you how awful you feel when you get that stuff. It's awful. I mean you just feel like you're going to die. This is your end result." Her test report contained technical data on the incidence of APOE-ε4 genotype in dementia patients – information obviously intended for a physician, not a layperson receiving the test report at home. The report also contained a disclaimer that the test was not useful for predictive purposes in asymptomatic subjects. Claire received no genetic counseling and little help in interpreting the result. (This lack of counseling was apparent in, e.g., Clare's perception that both the ε3 and ε4 forms of APOE conferred extra risk of AD. She actually had a lower risk than she realized.)

Claire resolved to tackle the problem aggressively. Already a vegan and long-time runner, Claire threw herself into research on diet and dietary supplements and now takes roughly fifty supplements purported to promote health and cognition. Clare is also making preparations for the possible onset of the disease, by which she means preparations for suicide. "I'm actually a really happy person most of the time. But there's this . . . depressive presence over me every day. I think about it every day. . . ." She has looked at real estate in Oregon, where physician-assisted suicide is legal. She collects ideas of methods she thinks she could use, and referred to several of them in the course of her interview. She speaks passionately about the indignities her mother endured in long-term care facilities (she calls them "hell holes") and equally passionately about the right to die with dignity.

Despite this daily contemplation of self-euthanasia, when asked what she would do if she could go back and make the choice to get tested again, she said she would do it. "I just think knowledge is power." When asked how she would advise others contemplating APOE testing, Claire said that it "depends upon your emotional fragility. It depends upon whether you're a person who likes to gather information to protect yourself." Describing a friend who defers to physicians for health information, she emphatically added: "I say, *screw* the doctors. Take control here. . . ! Find *out!* . . . I know *much* more about this disease than the general G.P. Just because I dive *in!*"

"Josh"

Josh is in his forties and works for a large private medical research organization. Recently, his employer initiated a study of the effect of genetic susceptibility testing on health behavior and urged employees to participate. Josh saw no harm in it. Why not do something

for science? Also, he thought, he had somewhat elevated blood glucose levels in his last physical examination. He wondered if he had a predisposition to type II diabetes. With a bachelor's degree in biology, experience as an emergency medical technician, and daily exposure to issues in clinical medicine at work, Josh thought it might be useful to find out.

The clinical study organizers had an arrangement with a DTC testing company to provide health-related genetic testing for participants. According to the DTC company's online FAQs, study participants would receive "detailed genetic screening [that] will assess individual genetic risk for more than 20 health conditions that might be altered by lifestyle changes." Individual lifestyle patterns would then be tracked through self-assessment questionnaires administered by Josh's employer. If desired, participants could seek genetic counseling from the DTC company after receiving their results. Josh reviewed and signed the online consent form and sent off his saliva sample.

Weeks later, the test results arrived. Josh did not have a predisposition to type II diabetes. To his dismay, however, the report said that he had two copies of the APOE-ε4 allele, strongly predisposing him to Alzheimer's disease. He says the result "shocked the crap out of me. . . . I was not prepared for it emotionally." It was only now, retrospectively, that he thought about his family history for AD. Josh's maternal great-grandmother and numerous maternal great aunts and great uncles had had dementia. His mother was as yet asymptomatic – a fact which had made it easy to ignore the AD pervading his extended family. Josh's father had also recently been diagnosed with "mild cognitive damage." Was that related?

Josh called the DTC company's genetic counselor to find out more about the result. The advice was to eat healthfully and exercise. "Well, you know, *diet and exercise*. Well, what does *that* mean? Everybody should be . . . having a healthy lifestyle. What is this going to do?" Josh wanted to see clinical studies linking specific preventive measures to specific outcomes. In his hunt for information, he received a referral to a representative of the Alzheimer's Association. Again, he was told, diet, exercise, and "maybe some curry would be good." Josh reacted with skepticism. ". . . I'm like, okay, how much curry? [Laughter] Yeah! I mean, do I need to eat ten meals of curry of a day? *One* meal of curry? There was *dis*information out there. . . ."

Josh was likewise frustrated that the interpretation of the test result itself seemed unclear. "The company that did the test put my risk at 69% where a Duke University study [put it] at 91% . . . ." What was he supposed to believe? He went to his primary care physician "who kind of looked like a deer caught in the headlights because he had no clue that this was coming down the pike. I actually had more information for him than he had for me." Josh also had a few sessions with a psychologist "because I felt like here I was given something and I didn't have any control over it. And where do I go? What do I do?"

In the end, Josh began using nutritional supplements, using a treadmill, doing cognitive exercises, and eating a Mediterranean diet. He does these things with skepticism, not hope. Several months after his APOE disclosure, his sense of disempowerment and abandonment has not abated. He feels let down by a system that allowed him to have this information when preventive measures are unproven and help is lacking in sorting inflated claims from real health data. He speaks forcefully about the direct-to-consumer industry that perpetrates this seeming injustice. "It just boggles my mind. . . I can't go into a laboratory and say, 'I think I have an infection. Can you please draw CBC on me?' [They'd] say, 'No, we have to have a physician's order.' And yet *anybody* can submit a saliva sample and get their genetic testing, which clearly is medical information. . . . I question whether it's ethical or not to be done that way."

When asked what advice he would give to a hypothetical friend considering testing, he initially said he would want to "make sure that they're pretty well aware of actually what they're getting into." A few days later, Josh re-contacted me asking for a supplemental interview. In that interview, he said, ". . . I would *not* recommend this procedure or testing to anybody" because, in the first place, "there really isn't anything you can do about it." Plus, he has not found any ongoing prevention trials for asymptomatic patients at risk for AD. So, he concluded, "it really doesn't help, one way or another, to know this information."

Josh's retrospective assessment of the informed consent process is damning. He believes there should have been a face-to-face informational session, either individually or in a group, to provide prospective participants with pre-test genetic counseling. He was adamant that if the process had included genetic counseling, especially directed reflection on family histories prior to testing, he would *not* have chosen to participate. He wishes fervently that someone had said, "Right now [with AD] there really isn't anything you can do that we know that will make a difference in your outcome. So therefore do you *really* want to know this?" He feels that the clinical trial organizers abdicated their responsibility to provide adequate safeguards for participants by defaulting to the DTC consent process, which failed to prepare him for the result. Josh yearns to call attention to what he sees as arrogant disregard for the employees his company herds into its study, some of whom will unwittingly receive APOE-ε4 disclosures like him. He remains silent for fear of losing his job.

Meanwhile his family downplays the importance of the result. "I mean, [my wife] is like, 'it's no big deal.' But they've never lived with Alzheimer's. They've never seen it. So I told them . . . *you're* going to be suffering from this if I get sick! It's going to affect *you* more than it's going to affect me at some point in time." His efforts to make them face the reality of AD have strained his marriage and family life. Powerless to mitigate his risk of AD, invalidated at work and at home, Josh told me, "I feel at this point in time that I've been harmed by this and not helped by this." Despite the changes he claims to have made to his lifestyle, he is gaining weight. "I'm just left with anger. . . . I'm just left with anger."

The Yin and Yang of APOE

The two subjects discussed here are both well educated, one with a background in healthcare. Both of them have strong family histories of dementia, but neither was conscious of that history until forced to confront it. One subject specifically sought out her APOE genotype, the other got the information coincidentally. Both subjects are APOE-4 positive, and both expressed similar reactions to this news (shock, dismay, a desire to gather information and intervene proactively). Yet one of them feels empowered and would do the testing again, while the other feels disempowered and regretful.

Significantly, Josh feels harmed by this unwanted knowledge. He lives each day with seething anger and a sense of profound abandonment. Even Claire, who says she feels empowered, describes a "depressive presence" clouding her daily life fully *seven years* after her APOE disclosure. Part of this "presence" no doubt has to do with the literal presence of her mother, now in a vegetative state, whom Claire has at home. Josh currently lacks that burden, but also lacks Claire's sense of proactive control. His long-term outcome remains to be seen, but his near-term distress is of concern.

Multiple factors contribute to the differing attitudes expressed by these two people, including their educational backgrounds and attitudes towards what constitutes valid knowledge. Claire's "knowledge" is often Josh's "disinformation." Nevertheless, despite the lifestyle interventions they embrace to varying degrees, both subjects harbor a relatively gene-based view of AD risk. By contrast, the heavily counseled REVEAL participants

tended to fall back on traditional views of "blended inheritance" to assess their personal risk (Lock, *et al*. 2006); ultimately, genotype information did not significantly modify their pre-existing views of inheritance and risk.

Importantly for this discussion, the difference between the two subject's attitudes is clearly related to the manner in which the APOE disclosure was obtained. Claire had the opportunity to learn about APOE and to consider carefully what it would mean to her. Although Claire underwent no formal consent process, she sought APOE testing knowing she would receive AD risk information and understanding why she wanted it. Hence, her decision was reasonably well informed. Josh, on the other hand, was blindsided by a result he never consciously sought. In this age of genome-wide association studies, researchers fret over what kind of information subjects should be given (McGuire and Lupski 2010), in part because they wish to avoid situations like this one. Blind to his extended family history and distracted by his concern over predisposition to one particular disease, Josh gave little thought to the other 21 diseases offered in the testing package when he decided to participate. As Josh said in his interview, ". . . it just wasn't on my radar screen." Although Josh underwent a formal consent process, his consent was not well informed because he could not envision the practical implications of the results he might get.

DTC Genetic Testing and Consent

The responses Claire and Josh had to their APOE disclosures were conditioned by the degree to which each of them was able to reflect on the implications of the information they were about to receive. It follows that the pre-test information given to prospective APOE test-takers should prepare them for the possible real-life consequences of the test results. But what happens to informed consent when health information is offered as a consumer product? Human subject research regulations do not extend into this arena, hence Federal guidelines for "informed consent" do not apply. Intuitively, given the disease-related information they sell, we might assume that genetic testing companies are under FDA oversight. However, the Agency's role is limited. In the US, DTC genetic testing is considered general commerce, where communication of information to promote the sale of lawful products or services – "commercial speech" – is overseen by the Federal Trade Commission (FTC) (Javitt, Stanley, and Hudson, 2004). In this realm, commercial speech is protected under the First Amendment; the courts have barred content-based prohibitions of commercial speech, even in matters concerning public health (Ibid., 287).

This is a crucial distinction: the information provided by DTC testing companies at their websites is *not* comparable to the information provided by clinical physicians or researchers for informed consent. The former is commercial speech, designed to sell a product. Of course, under the Federal Trade Commission Act (15 USC Sec. 41–58), unfair or deceptive acts or practices are unlawful. However, there are no specific requirements for disclosure of risks and benefits as there are for human subject research (45 CFR 46). With general commerce, we have informed *choice*, not informed consent, and the information requirements differ.[4]

FTC policy on deceptive communication practices (FTC 1983)[5] dictates that a deception exists "if there is a representation, omission or practice that is likely to mislead the consumer acting reasonably in the circumstances, to the consumer's detriment" (Sec. I). Under this policy, the question is *not* whether an act or practice causes actual deceptions, but whether

[4]See the contrast Berger and Twerski (2005) make between informed consent in medical malpractice and informed choice in product liability cases. In that context, the term "informed choice" has a specific legal significance and history. My use of it here is more generic, but a useful way to discuss the issue.

[5]See also the discussion in Javitt, Stanley, and Hudson, 2004.

the practice is *likely* to mislead (Sec. II, emphasis added). Importantly, a "material" misrepresentation or practice "is one which is likely to affect a consumer's choice of or conduct regarding a product" (Sec. IV); likewise, injury exists "if consumers would have chosen differently but for the deception" (Ibid.). Moreover, the Commission "considers claims or omissions material if they significantly involve health, safety, or other areas with which the reasonable consumer would be concerned" (Ibid.).

With these policies in mind, let us return to the cases under discussion. Josh's DTC genetic testing company provides a great deal of disease-specific information at its website. However, as discussed earlier, the diseases in the testing package vary widely in terms of their interpretation and real-life implications. Consider the chasm of emotional and physical impact between prophylactic radical mastectomy to prevent breast cancer as compared with the diet, exercise, and medications prescribed to prevent heart attack. Combine the complexity of this information with the fact that even a relatively sophisticated user (like Josh) is likely to have preconceptions regarding which diseases are a matter of concern, and it becomes clear that our hypothetical customer is extremely unlikely to consider the consequences of all possible (or even probable) outcomes, and ill equipped to do so. If informed consent for multiplex testing in a clinical context is problematic, as some authors have observed (AMA 1998), then in the DTC environment informed choice is virtually impossible to achieve.

For these reasons, bundling heterogeneous testing products into complex portfolios of health-related risk data constitutes a practice likely to mislead consumers acting reasonably under the circumstances. It is not that the companies (necessarily) intentionally deceive, but that the practice of bundling inevitably leads to de facto material omissions and misapprehensions.[6] The "deception" at the heart of these information practices is material on two counts. First, Josh is adamant that if the company had provided information in a directed, more digestible format, he would have made a different choice. Second, a gravely serious health concern of importance to consumers is at issue (vividly illustrated by Claire's daily contemplation of self-euthanasia). Under the current practices, injury is likely; some subset of DTC customers will inevitably receive unexpected and bitterly regretted news coincidental to the information they consciously sought – a phenomenon which, in a different context, has been called "inflicted insight" (Baumrind 1979).

To put this statement into perspective, let us return to our "worst case" of Alzheimer disease. In a recent "webinar"[7] Dr. Robert Green noted that in the REVEAL trial, 24% of first-degree relatives of people with Alzheimer's disease who were "systematically obtained" (as opposed to self-referred) expressed interest in learning their APOE genotype. Green observed that if this percentage holds true for the overall population of first-degree relatives of people with AD (40 to 60 million people, according to Green's guess), then 10 to 15 million people might want APOE testing – a figure he found "staggering." If true, the flip side of this statistic is more impressive: 76% of first-degree relatives contacted for the study ultimately did *not* want to learn their APOE genotype – which, using Green's estimates, leaves us with 30 to 45 million people who would *not* want to know.

Moreover, as an anonymous referee for this journal usefully noted, the population in the REVEAL study were overwhelmingly white, relatively affluent, and registered volunteers for participation in AD research studies. This group likely *over-represents* the number of

[6]The FTC also has standards for "unfair" practices, which might seem to apply here. However, the technical definition of "injury" resulting from unfair practices is primarily monetary (FTC 1980). Hence, FTC rules for misleading communication practices fit the case of genetic test packaging better than the rules for unfair business practices.

[7]Genetic Alliance, "From risk assessment to lifestyle choices: what does it mean to be a previvor?" [Webinar] 22 July 2009, 12:00 - 1:00 pm ET, http://www.geneticalliance.org/webinars-genetics-advocacy (accessed February 11, 2011).

people interested in APOE testing. And among the many millions of first-degree relatives who would refuse APOE (importantly, a group in which the number of APOE-ε4 carriers is enriched compared to the general population), it is reasonable to believe that some proportion would, like Josh, feel harmed rather than helped by a coincidental APOE disclosure.

Conclusions and Recommendations

Under the current legal regime, complex, confusing, or relatively meaningless genetic data is for sale. Other authors have rightly called for improved data standards and oversight (e.g., Robertson 2009). My concern here has been to assess two actual contrasting cases of consumer genetic testing in light of currently applicable law. The cases show that pre-test comprehension of the disease-specific, real-life implications of possible test results is crucial for avoiding consumer injury, particularly where incurable, fatal diseases are involved. DTC websites do provide much disease-related information. However, this information constitutes commercial speech having commercial purposes, and should not be construed as contributing to informed consent. Even the clinical researchers in charge of Josh's clinical study misconceived this fundamental distinction and delegated experimental informed consent to the DTC company.

How can we protect consumers from the inflicted insight of an unwanted APOE (or other) disclosure? We cannot censor commercial speech, but we can require it to be reformatted for greater clarity by disaggregating the standard packages of health-related genetic tests offered on a DTC basis. Whatever marketing or economic rationale may underlie this service bundling, that rationale is trumped by the problems of informed choice described above. Of course, some companies offer the standard package but allow customers to opt out of certain disease indications. However, the same blind spots and preconceptions which confound informed purchase in this context also preclude an informed choice for opting out. It is preferable for customers to opt *in:* to select diseases from a menu, ordering a la carte and paying per disease (or at most, selecting from small portfolios of disease-related tests having comparable implications for counselling).

In this way, the customer actively sets the parameters for the information she will receive; she is forced to make a conscious choice and is less likely to be frivolous in selection since each test is priced separately. Rather than a single generic "consent" form, the information provided should be tailored for the tests chosen; information pages for each selected disease should be presented as part of the ordering process, prior to completing the transaction. The customer should have to confirm review of each page before continuing. For a fatal and incurable disease like AD, I would also advocate a mandatory *pre-test* conversation with a genetic counselor to explore family history and clarify any ambiguity about treatment or prevention of the disease.

This last suggestion may be especially problematic since DTC testing companies often entice consumers by offering hope of preventing disease.[8] While writing this article, I searched Google for "Alzheimer's prevention." A sponsored link for Navigenics appeared at the head of the page declaring: "Get tested for Alzheimer's & learn how you can Prevent Alzheimer's."[9] This kind of advertising undermines effective informed choice for AD testing (and essentially constitutes a "bait-and-switch," since the company cannot actually deliver proven AD prevention strategies). Yet, to date, the FTC's only response has been to

[8]Many observers have noted the problematic and exaggerated marketing claims often made by DTC companies. See, e.g., Hull and Prasad 2001, Gollust, Hull and Wilfond 2002, Gray and Olopade 2003, Bowen, Battuello and Raats 2005, Williams-Jones 2006.
[9]Search performed on July 24, 2009.

post a consumer advisory webpage called, "At-Home Genetic Tests: A Healthy Dose of Skepticism May Be the Best Prescription."[10] Perhaps consideration of the fundamentally misleading nature of DTC test packaging would motivate the FTC to revisit the issue. With increased scrutiny, DTC companies may be compelled, voluntarily or otherwise, to modify their packaging, informational, and marketing practices for better informed consumer choice.

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References

ACMG (American College of Medical Genetics, American Society of Human Genetics and Working Group on ApoE and Alzheimer Disease). Statement on the use of apolipoprotein E testing for Alzheimer disease. Journal of the American Medical Association. 1995; 274 (20):1627–1629. [PubMed: 7474250]

ADI (Medical and Scientific Advisory Committee and Alzheimer's Disease International). Consensus statement on genetic testing for Alzheimer disease. Alzheimer Disease and Associated Disorders. 1995; 9 (4):182–87. [PubMed: 8749605]

AMA (Council on Ethical and Judicial Affairs, American Medical Association). Multiplex Genetic Testing. Hastings Center Report. 1998; 28 (4):15–21. [PubMed: 9762534]

Baumrind D. IRBs and social science research: The costs of deception. IRB: A Review of Human Subjects Research. 1979; 1 (6):1–4.

Berger MA, Twerski AD. Uncertainty and informed choice: Unmasking Daubert. Michigan Law Review. 2005; 104 (2):257–290.

Bird TD. Genetic aspects of Alzheimer disease. Genetics in Medicine. 2008; 10 (4):231–239. [PubMed: 18414205]

Bowen DJ, Battuello KM, Raats M. Marketing genetic tests: Empowerment or snake oil? Health Education and Behavior. 2005; 32 (5):676–85. [PubMed: 16148213]

Evans JP, Skrzynia C, Burke W. The complexities of predictive genetic testing. British Medical Journal. 2001 April; 322 (28):1052–1056. [PubMed: 11325775]

Farrer LA, et al. Effects of age, sex, and ethnicity on the association between apolipoprotein E genotype and Alzheimer disease. A meta-analysis. APOE and Alzheimer Disease Meta Analysis Consortium. JAMA. 1997; 278:1349–1356. [PubMed: 9343467]

FTC. FTC Policy Statement on Unfairness. 1980 December 17 [accessed June 10, 2010]. http://www.ftc.gov/bcp/policystmt/ad-unfair.htm

FTC. FTC Policy Statement on Deception. 1983 October 14 [accessed June 10, 2010]. http://www.ftc.gov/bcp/policystmt/ad-decept.htm

Gatz M, et al. Role of genes and environments for explaining Alzheimer disease. Archives of General Psychiatry. 2006; 63:168–174. [PubMed: 16461860]

Gollust SE, Hull SC, Wilfond BS. Limitations of direct-to-consumer advertising for clinical genetic testing. JAMA. 2002; 288 (145):1762–67. [PubMed: 12365961]

Gray S, Olopade OI. Direct-to-consumer marketing of genetic tests for cancer: Buyer beware. Journal of Clinical Oncology. 2003; 21 (17):3191–93. [PubMed: 12874271]

HHS (U.S. Department of Health and Human Services, National Institutes of Health and National Institutes of Aging). Can Alzheimer's Disease be Prevented?. 2009 [Accessed 4 February 2010].

[10]http://www.ftc.gov/bcp/edu/pubs/consumer/health/hea02.shtm (accessed June 10, 2010).

[online]. NIH Publication No. 09-5503. Available from: http://www.nia.nih.gov/alzheimers/publications/adprevented/

Holtzman NA, et al. Predictive genetic testing: From basic research to clinical practice. Science. 1997; 278(5338):602–5. [PubMed: 9381169]

Hull SC, Prasad K. Reading between the lines: Direct-to-consumer advertising of genetic testing. Hastings Center Report. 2001; 31 (3):33–35. [PubMed: 11478123]

Javitt, GH.; Hudson, K. Issues in Science and Technology. 2006 Spring. Federal neglect: Regulation of genetic testing; p. 59-66.

Javitt GH, Stanley E, Hudson K. Direct-to-consumer genetic tests, government oversight, and the First Amendment: What the government can (and can't) do to protect the public's health. Oklahoma Law Review. 2004; 57(2):251–302. [PubMed: 15658034]

Lock M. Eclipse of the Gene and the Return of Divination. Current Anthropology. 2005; 46:S47–70.

Lock M, et al. When it runs in the family: Putting susceptibility genes in perspective. Public Understanding of Science. 2006; 15 (3):277–300.

Marteau, T.; Richards, M., editors. The Troubled Helix: Social and Psychological Implications of the New Human Genetics. Cambridge, UK: Cambridge University Press; 1996.

McGuire AL, Lupski JR. Personal genome research: what should the participant be told? Trends in Genetics. 2010; 26(5):199–201. [PubMed: 20381895]

NIA (National Institute on Aging and Alzheimer's Association Working Group). Apolipoprotein E Genotyping in Alzheimer Disease. Lancet. 1996; 347 (9008):1091–1095. [PubMed: 8602063]

Parthasarathy, S. Building Genetic Medicine: Breast Cancer, Technology, and the Comparative Politics of Health Care. Cambridge, MA and London, England: The MIT Press; 2007.

Pollack, A. Walgreens delays selling personal genetic test kit. New York Times; 2010 May 13. p. B5

Roberts JS, et al. Who seeks genetic susceptibility testing for Alzheimer's disease? Findings from a multisite, randomized clinical trial. Genetics in Medicine. 2004; 6(4):197–203. [PubMed: 15266207]

Robertson AS. Taking responsibility: Regulations and protections in direct-to-consumer genetic testing. Berkeley Technology Law Journal. 2009; 24:213–243.

Seripa D, et al. Alzheimer disease risk associated with APOE4 is modified by STH gene polymorphism. Neurology. 2004; 62:1631–1633. [PubMed: 15136700]

Tsuang DW, Bird TD. Genetics of dementia. Medical Clinics of North America. 2002; 86 (3):591–614. [PubMed: 12171060]

Wachbroit RS. The question not asked: The challenge of pleiotropic genetic tests. Kennedy Institute of Ethics Journal. 1998; 8 (2):131–44. [PubMed: 11657425]

Williams-Jones B. 'Be ready against cancer now': Direct-to-consumer advertising for genetic testing. New Genetics and Society. 2006; 25 (1):89–106. [PubMed: 17312631]