

I Had Genetic Testing for Alzheimer's Disease Without My Consent

Anneke Lucassen

My mother has Alzheimer's disease. Her mother did too. Neither was particularly young when symptoms could no longer be hidden from the outside world, but both were remarkably intelligent and progressive women before the illness struck, so the change was dramatic.

If you google "should I have a genetic test for Alzheimer's disease" the general consensus is an emphatic 'no'. In fact, scrolling through the first two pages of hits after this search, I couldn't find a single site that recommended such testing. Most professional organisations that have proclaimed on the issue say no—for example, The Fisher Center For Alzheimer's Research Foundation says, "[It] should always be done with a genetic counsellor that will be available to discuss test results."

Yet my sister and I had a genetic test for Alzheimer's without ever giving a blood or saliva sample, and without being asked if we wanted it. Here's how it happened:

In the summer of 2013, a relative of mine got a good bulk deal on some "23andMe" genetic testing kits and decided that genetic testing of various family members would be interesting. Several of my cousins, aunts and uncles were tested. I wasn't

offered a kit—perhaps they knew I would be skeptical, perhaps because they just didn't get round to asking me, as we live in different countries. The first I heard about any of it was when my father told me that the results of genetic testing in him and my mother had diagnosed the two conditions they both had correctly. "How so?" I asked, and the story of the 23andMe kits unfolded.

All they had had to do was spit into a pot and soon afterwards "a lot of very interesting results came back." Did my mother know that she was having genetic testing? Well no, but she was happy to spit into a pot and could see my father doing so, and it didn't involve needles or anything. Not a lot of effort and "it's really a very good test" he said. Not only had the test said that my mother had a roughly 40% chance of developing Alzheimer's, it had also said my father had a roughly 33% chance of developing a deep vein thrombosis (DVT), and he'd had two of those!

I felt confused. On the one hand I wanted to dismiss these results as too vague, with insufficient evidence to support them, on the other, the scientist in me wanted to know more, and find out how 23andMe had come to these conclusions. My father forwarded my aunt's login details and soon I was looking at the results of about 16 relatives including those of both my parents. According to 23andMe, the test offers genetic testing of some 900,000 locations throughout the genetic code. Given that much of our genetic code is the same (on average humans are 99.9% identical) the test homes in on known variable spots 'SNPs' or single nucleotide polymorphisms throughout the three billion nucleotides (or "letters") of our genetic code—the code we inherit from our parents—and then looks at published data that has explored disease risks associated with different variants.

I had expected that the results would be much vaguer than my father's impression once I looked at the actual data, but was shocked to see that my mother's chance of Alzheimer's disease was estimated to be 40%. My surprise was not about Alzheimer's—this had already been diagnosed some years earlier—but I had always thought the condition to be multifactorial and not so predictable.

from a genetic code. A combination of multiple, individually weak, factors with as the end result the disease. I had thought that environmental factors-such as boiling rhubarb in aluminum pans in the 1970's, enjoying her tipple, smoking, and frying food in butter-were the biggest culprits. But this result suggested that there was something in her genetic code, something she was born with, that meant her chances of developing the condition were always much, much higher than average. Of course, she was also born with a 60% chance she would never develop it-but even so, the magnitude of the risk associated with this single gene variant surprised me.

I found myself digging deeper; I wanted to see what this prediction was based on. The 23andMe website has a lot of information but is quite easy to navigate. Although I knew that a genetic variant in the ApoE gene (which encodes a protein apolipoprotein E), was a risk factor in Alzheimer's I was surprised to find that my mum has two copies of the high risk variant , or ApoE4 allele; she is "ApoE4 homozygous", which only 3 in every 100 people of European ancestry are. Having two copies is not enough to cause it, or indeed diagnose it, but the E4/E4 combination is the strongest genetic predisposition known for late onset (after the age of 65) Alzheimer's. As I was looking at this result, I realized the implications for myself, without ever thinking, "do I want to know this?" I must have inherited one E4 variant from my mother, since that was all she could pass on to me. Did I also have this bad combination of two E4 alleles? Was I born with this eight fold higher than average risk? My father's result might help clarify. His result was even more unusual: he has two copies of another variant of the ApoE gene: the ApoE2 allele-only 3 in every 1000 people of European ancestry have this result. There are three variants in question; ApoE 2,3, and 4, and most-about 95% of people, of European descent have either two copies of E3, or an E3 in combination with E2 or E4.

Shortly afterwards the penny dropped. I could only have 'one possible genotype-as could my sister. We were both E4/E2 heterozygotes and could only have inherited this possible combination. You

might think that I chose to find this out, but it didn't feel like that to me. It was only after the event that I thought that maybe I could have chosen not to look. At the time, without realizing what I was doing, I was getting results without giving a sample, asking for a test, or specifically consenting to a test.

A year or so later, what do I think about this? Well on the one hand I think it's no big deal. I found out something without setting out to find it, but it hasn't made me "freak out and become clinically anxious or depressed"-one of the reasons "most doctors" say you should not get tested for a gene that puts you at high risk of late onset Alzheimer's, according to a medical website. Also, knowing I have only one ApoE4 allele is much better than two in terms of my risk, but most of the sources I looked at said that the risk of Alzheimer's was still higher with one ApoE4. James Watson specifically excluded information about ApoE status when he published the results of his genome analysis, so it was information he didn't want others to know, or he thought making this public would somehow disadvantage him. Living in the UK means that I know that I currently do not need to tell any insurance body about this finding, but might I be disadvantaged in any other way?

One of the reasons most professional guidelines say that we should not test for Alzheimer's risk through ApoE4 status is that there isn't anything that can be done to prevent or treat the condition-or at least anything you would do differently on the basis of the test result. The test doesn't alter clinical management. But would that recommendation change if it did? A study from Stanford published in 2013 suggested that Hormone Replacement Therapy (HRT) in women who carry an ApoE4 allele were protected from Alzheimer's whilst it had no discernible effect in those who did not. Should I therefore take HRT, knowing that I must have an ApoE4 allele? I haven't asked the researchers directly, but I suspect the answer would be along the lines of "too early to tell, further research needed." I asked my GP for advice. She hadn't heard of these studies but readily took out her prescription pad whilst I was talking. But have I also inherited my father's tendency to DVT, which would be a contraindication to HRT? And in any case how

strong would any 'tendency' have to be to take out preventative actions even if there was enough evidence? Would a 20% lifetime risk be high enough? The 23andMe website tells me that "knowledge is power" but that felt increasingly like a rather hollow slogan: what power do I have, and to do what?

These are complex decisions which I found all the more difficult because I did not set out to make them. Of course, we often don't get to choose when we have to make decisions about our health, but they are usually made because of signs or symptoms we know about, or on the basis of our own medical test results. It felt very strange to be thinking about all this when I'd never even had a test, and had always thought that I wouldn't choose to find out if I had inherited a tendency to an untreatable disease.

23andMe is a direct to consumer company that allows the customer to bypass their health professional and find out about certain health risks indicated by their genetic code. Its website headline is "Find out about your ancestry and your health" although confusingly the health component has been suspended in the USA since late 2013 because of FDA restrictions but health information gleaned from testing before that date remains on the website. However, a recent European launch includes both health and ancestry predictions, presumably because Europe lies outside the FDA's jurisdiction. But is lumping the two together confusing? Knowing whether I am two or three percent Neanderthal, or have some Scandinavian ancestors, seems qualitatively different to predicting diseases I am likely to get. My relatives took part because they thought it would be 'interesting' and being a generally open bunch thought nothing of sharing information more widely. But would information about my mother's genetic Alzheimer predisposition not be better and exclusively kept in her confidential health records? That way, I could only find out about my genotype if I had wanted a test myself or got specific consent from both my parents to examine their genotypes. I did neither. We hear a lot about new genomic technologies 'personalising' our healthcare and giving us the knowledge to learn more about ourselves, but perhaps what we might learn about family members should also receive attention? That way,

we might consider taking more time to think about delving into familial information before doing so. The 23andMe website says "Your family may or may not want to know [hereditary] information as well, and relationships with others can be affected by learning about your DNA" but is this sufficient for people to be able to properly consider the potential familial consequences?

I'm not calling for new rules or laws, and I don't think that anyone did anything wrong here, but the familial implications and consequences do seem to be somewhat brushed under the carpet in the great genomics PR machine. Surely this is something we need to consider more? But in calling for this, and in narrating my story, I raise another issue: By writing about this I have made public the story of my mother's illness. Is this invading her privacy at a time she can no longer tell me she would rather I didn't publish this story? All I can say is that I think she would have approved and would have welcomed more debate about the downstream implications of quick and cheap genetic testing. I hope I'm right.