The dark side of direct-to-consumer genetic tests
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By Natasha Cowan

Direct-to-consumer testing is an affordable way to better understand your DNA, but is this a leap forward in innovation or another layer clouding an already complex market? From anxious patients to unnecessary surgeries, we reveal the barriers for healthcare professionals and patients, and how to solve these industry challenges.
Today, anyone with £150 can order a genetic test from the comfort of their own home. These tests promise to unlock the secrets of consumers' DNA, reporting on genetic health risks, carrier status, traits and ancestry.

This is the Uber of healthcare, catering to millennials’ desire for slick websites, wellness-trends, and neatly packaged information delivered at the click of a button. However, with a recent study revealing 40% of the raw data produced in direct-to-consumer tests is incorrect, there is a question mark over how far these tests are benefiting patients or if they are clouding an already complex market.

Blue Latitude Health speaks to two experts in the field of genetic testing to learn about this issue and better understand how the industry can unite to solve these challenges.

THE LIMITATIONS OF DIRECT-TO-CONSUMER GENETIC TESTS

Some of the leading direct-to-consumer genetic testing companies use third-party sites to analyse data. However, this data is not always up-to-date or correct. Now new evidence has emerged showing that an “alarmingly high” 40% of raw data delivered by third parties analysing direct-to-consumer tests is incorrect.

Rather than providing a comprehensive genetic risk assessment, these tests analyse a limited set of variants, which are not necessarily causal of conditions. The tests do not consider the impact of environment and lifestyle. Instead, they interpret single-nucleotide polymorphisms (SNPs), and while SNPs can indicate a gene is associated with a disease, many are benign and have no impact on health.

While this may be clear to those with a background in genetics, the lack of public awareness around genetic science combined with the limited genetic knowledge healthcare professionals possess, provides a perfect storm of risk for patients.

GENETICS: ONE PIECE OF A COMPLEX PUZZLE

In 2017 the FDA approved the first direct-to-consumer genetic test. However, the approval came with a caveat preventing test results being used to ascertain a consumers’ overall risk for developing a condition.

Still, everyday members of the public order these tests, receive the results and visit their doctors to decipher the information, despite the disclaimers and warnings.
Who can blame them? If an email landed in your inbox that appeared to indicate you had an increased risk of cancer, Parkinson’s disease, Alzheimer’s disease, or any other potentially life-altering or life-threatening condition, you would want to confirm the results with a healthcare professional too.

Taichi Ochi is a Regional Account Manager at *Macrogen*, a Korean biotech and precision medicine company that specialises in next-generation sequencing. The organisation works across 153 countries. Its services range from conducting government research to providing patients and healthcare professionals with diagnostic results, offering genome studies and using genomics in forensics. To date it has completed 30 million cases of genome sequencing, making it a market expert.

For Taichi, the challenges of direct-to-consumer tests should come with a warning: “while the tests are a great asset for healthcare, it is not the bible that people should refer to when making clinical decisions. Using direct-to-consumer tests as the main source of decision making is the same as identifying the completed puzzle from a puzzle piece”

**WHAT IS A VARIANT OF UNKNOWN SIGNIFICANCE (VUS)?**

One of the barriers around direct-to-consumer testing is the lack of education on genetic variants held by both physicians and the general public.

“Patients are frequently confused by what a variant means. They often misunderstand and think a variant means they have got a disease-causing mutation, which isn’t right” says Vicki Kiesel, a Director at *GeneHealthUK* with a decade of experience in genetics.

“I explain variants to patients using bad analogies. For example, I use the word ‘colour’ and explain that in England we include a ‘u’ but in America, it is spelled without a ‘u’. Neither are bad, they mean the same thing, and that’s what a variant can be.

“We compare genes to a standard template and because we’re all different, we have these changes; some of these are harmless and some can cause disease. You can use terrible analogies or explain it all in scientific detail but psychologically, all the patient hears is that there is a change in the genes they’re worried about”

To further confuse things, the direct-to-consumer test results do not consider false positives. As a result, some consumers feel unnecessarily worried. Meanwhile, others who are predisposed to a condition can receive false results, leaving them feeling they have no chance of developing a disease.

Vicki has seen the impact of this first hand, ranging from mildly confused patients
to harrowing results for a patient’s health. “False negatives and false positives from direct-to-consumer genetic tests are definitely something I’ve come across, and every clinician in genetics comes across now,” Vicki reveals.

“For example, one prominent company only tests for the mutations in the BRCA genes that occur in the Ashkenazi Jewish population. However, the public doesn’t understand what this means. That’s one of the challenges of not having a genetic professional available to discuss the results in person with a patient. It means people from non-Jewish ancestry can think they’ve been tested for mutations in the BRCA genes when reality they haven’t – the test they had is meaningless for them.

“We only see them when someone else in the family has been tested and learned that they have the genes, or if they have developed breast cancer themselves. They think they have already been tested so they wonder why they have breast cancer at all.”

UNDER THE KNIFE
While a rare occurrence, Vicki has met patients who have had unnecessary surgical procedures due to incorrect interpretation of test results.

“I have met patients who have had mastectomies because of genetic variants of unknown significance, which were not a mutation. Now, in many regions, the NHS asks someone from genetics to look at the result to make sure doctors aren’t acting on a variant.

“However, it’s ad hoc, it’s not standardised. Some people are still being treated as though they have mutations when they only have a variant.

“The impact on patients is incredibly traumatic,” she explains emphatically. “On one side, the patient’s been given the wrong information, and they believe they are not at increased risk, which is not medically safe.

“On the other side, patients’ have been over-treated, and that has huge psychological implications. Once you’ve told someone a variant is there, no matter how much you explain it, they think there is a change there, and that’s a problem.”

THE TOOLS HEALTHCARE PROFESSIONALS NEED
As public awareness of direct-to-consumer genetic testing grows, more patients are contacting physician looking for clarity and reassurance. Here, doctors have to make a call on whether or not to send the patient for further tests to follow up on information provided by a third party.

They will also be expected to integrate the risk information into a personalised holistic plan, that includes environmental factors and the family history. However,
often healthcare professionals do not feel confident in their knowledge of genetics, or in their counselling skills, as exemplified in the scenarios Vicki has previously experienced.

A recent cross-sectional survey of 50 obstetricians and gynaecologists found 74% did not feel comfortable counselling patients about available genetic testing for Lynch syndrome, and 76% didn’t feel comfortable counselling patients about such testing criteria. These concerns are preventing patients from receiving the best care and are providing a barrier to embedding precision medicines in healthcare systems.

“It’s human nature. No one wants to be given a death sentence or health warning by a kit provided by a third party. Patients’ want to be able to engage with the information, and healthcare professionals want to feel equipped to have the right conversations,” says Taichi.

“Some patients will visit their clinician armed with different sets of results from different direct-to-consumer companies. They will want to know which one is correct. “Often the doctor doesn’t have the answers. If they are a general practitioner or focused on a specific area not linked to the patient’s concern, they rarely have experience in reviewing genetic data.”

The human genome was first sequenced in 2003, and the science has moved in leaps and bounds since then, far outpacing the speed of medical education.

Many healthcare professionals are struggling to keep up with the fast-paced scientific developments.

This is especially challenging in oncology where each type of a tumour differs. The movement from classifying cancer by organ of origin to defining it by its molecular makeup is also introducing further complexity.

“It makes it very tricky for healthcare professionals encountering questions,” Taichi explains.

“You get gigabytes of data, but you have to understand what that means for a specific tumour.

“As much as we would like to say that in the future the data will be generated and turned into a nice page-for-page outlining the risks for healthcare professionals, we’re still just entering this new area.

“We need to start thinking about how smaller hospitals or even large institutions are going to deal with all of this information. How are they supposed to sift through all that when the current capacity is limited and there isn’t a standardised process across the different institutions handling data?”
TEARING DOWN THE IVORY TOWER

For both Taichi and Vicki, the solution does not only lie in encouraging consumers and healthcare professionals to use reputable laboratories and work with an experienced clinician. Surmountable effort must be made to encourage collaboration between genetic testing companies, consumers, healthcare professionals, genetic counsellors, and genetic sequencing companies.

“The ivory tower mentality in healthcare needs to be breached,” says Taichi. “It doesn’t matter how much healthcare professionals’ study genetics – it’s such a novel, fast-paced area. Genetic sequencing companies and genetic counsellors are the funnels that sift through the data. Better partnerships will drive the efficiency needed to ensure the patient doesn’t get over-sold or under-sold, or in the worst-cases needlessly paranoid about their health.

Macrogen is currently working with clinicians and the public to support them in making the right choices and ensuring the best standards of care. “Our ambition is to expand our outreach towards the general public and we have begun taking steps to achieve that,” Taichi reveals.

Alongside working with pharma companies and biotechs, this includes helping patients and clinicians to understand the basics of genetic testing.

Following the recent announcement that the NHS will offer tumour DNA screening for all new cancer patients, Taichi gave a powerful lecture on Metagenomics and the benefits of next generation sequencing.

“I explained that this isn’t voodoo magic. You as patients have an opportunity to understand things and it’s all your choice. You have to understand the whole process and make decisions, whether about things like sharing data and data privacy or about the genetic tests themselves.

“As a company, that’s a gap Macrogen want to bridge for both patients and healthcare professionals. We want to help them understand what these developments mean and that we have to work together to ensure everyone can live a healthy life.”

Blue Latitude Health understands complex markets and the impact these complexities have on multiple stakeholders, from healthcare professionals to patients and their carers.

Contact hello@bluelatitude.com to find out how we can help you develop these rich insights into your customers and market.
Vicki Kiesel is the Genetic Director of GeneHealth UK. She has 12 years’ experience in cancer genetics, leads a national team of genetic counsellors and provides teaching to healthcare professionals from all backgrounds.

Taichi Ochi is a Regional Account Manager at Macrogen, where he advises clients on next generation sequencing projects and market and sales strategy development.

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