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Commentary

The Pros and Comms of Gene Sequencing

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Abstract
Full-gene sequencing undoubtedly comes with its pluses and its minuses. In this article, the authors aim to weigh up the pros and cons not only from the point of view of the patient but also in view of the doctor's possible perspective. Either party may be for or against it for a variety of reasons – for example, a fear of knowing too much on the part of the patient, and concerns about possible over-treatment on the part of the healthcare professional. One thing is certain: the possibility of full-gene sequencing is here and here to stay. At the very least, doctors need to make patients aware of their options, while offering balanced advice.

Learning to Communicate

Communication is key in the modern world of medicine. Patients and healthcare workers are having more and more discussions to determine, by co-decision, the best treatment path for the individual [1].

There are, of course, problems with this in that many healthcare professionals (HCPs) are not up to speed with the more recent developments in, say, personalised medicine and its reliance on genetics, imaging and other complex factors [2].

Things are moving so quickly in so many fields, and it is difficult for an HCP to know absolutely everything, but we must try to improve this situation.

Also, while the internet has undoubtedly opened more doors to patient awareness, the downside is that so much information out there can be misleading and, therefore, so-called self-diagnosis can lead to unnecessary stress on the part of the patient.

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As argued elsewhere in this special issue, health literacy is extremely important on both sides of the treatment "fence." Ongoing education and training for HCPs is a vital component as we move forward with more individualised medicine [3].

A further problem, however, is that even the most savvy and up-to-date doctor, nurse or other HCP may not have the best chance to communicate in an optimal way, covering all the bases, given the workload and time constraints (10-min average consultation times in the UK and elsewhere, for example) [4].

Many doctors have the famous "good bedside manner," yet even the smartest of patients will sometimes fail to ask the right, direct questions. When he or she doesn't, the HCP may not have the chance to fill in the gaps due to the ticking of the clock.

There is also the matter of patients being a little frightened to ask for a second opinion (to which they are entitled), pushing a question if they don't understand the answer fully, asking about clinical trials and discussing their own medical data.

Even with the best will in the world from the doctor, it can be intimidating. Especially as the patient also has to contend with worrying about his or her condition in the first place.

There is nothing really new in that, and it should have moved forward by now, yet hasn't.

The Pros and Cons of Gene Sequencing

What is new, however, is the possibility of a patient undergoing full-gene sequencing. The price has come down significantly, although HCPs may be reluctant to recommend it for several reasons, and patients may also be reluctant [5].

Below are two hypothetical conversations. The first is between an HCP and an 18-year-old man (let's call him "John") who has been doing some reading on genetics.

John: Doctor, I'm interested in having my genes sequenced. My grandfather and one uncle both died young of heart attacks, although my father has a healthy heart. I want to know the risks. Also, two other relatives died from lung cancer in their mid-60s…

HCP: Do you smoke?

John: No.

HCP: Well, that one's easy. Don't start. You don't need gene sequencing for that.

John: Um, ok. What about the heart attack issue?

HCP: Many things contribute to the risk of heart disease: lack of exercise, obesity and the wrong foods, too much drinking, the aforementioned smoking… Just live a healthy lifestyle and you'll probably be fine and have a good, long life.

John: But my uncle did everything in moderation and still had a heart attack. He didn't even smoke! I just want to know what the risks are – whether there's something in my make-up that means that, whatever I do in the right way, I'm still high risk.

HCP: You'd really want to know 30 years in advance that there's a large chance of you having a heart attack? Wouldn't that give you too much stress, and stop you enjoying life? I'd have a heart attack myself, just thinking about it at your age.

And what if we found something else along the way? A propensity for a certain other cancer? None of us live forever – we'll all die of something. Why stress yourself out at such a young age?

John: But…

HCP: And what if you have kids? Then you'll spend your life as a father worrying about what you may have passed down to them. That's if you told your wife in the first place. And how would she feel?

Then, if you decided to have kids anyway, would you tell the children? Would they want you to? Just because you have the option of gene sequencing, doesn't mean you have to take

it. All the hundreds of generations before you managed well enough without that kind of foreknowledge.

John: But I want to do it. Just because I can, I guess.

HCP: Well, I can't stop you, but you won't be doing it through me, as I strongly advise against it. You're too young to need to know all this.

John: Ok, but…

And so on…

The next scenario involves an older man (Ted) in his late 40s. This time we have an HCP with a different view for different reasons.

HCP: Ted, I've been thinking, there are very good reasons why you should have your genes sequenced.

Ted: Eh? What's that, then?

HCP: In simple terms it means we can test your DNA and look for any problems that are likely to arise in the future, like a cancer that's lying dormant, prostate trouble, that sort of thing. In this way we can take preventative measures.

Ted: But I'm only 47, why would I want to do that? I'm as fit as a fiddle. Well, mostly. But I don't want to know that I'm going to die of leprosy or something at 82. I'd be counting down the minutes!

HCP: I understand that, but you're almost at an age when things can start to go wrong. I don't want to alarm you, as there is no current evidence regarding yourself, but we all have different genes and, these days, we can use them to target therapy to you personally, even before a disease flares up.

Modern methods mean, firstly, we can figure out the likelihood of you developing a certain disease and take early measures to manage it. Secondly, it will give us clues to the best treatment – for example, chemotherapy is a waste of time and resources in some cancer patients – and, thirdly, with your consent we could share your information, anonymously, to help other people down the line.

Ted: But I'm 47! Why not ask me in ten years?

HCP: Because now is a perfect time. Let's nip any potential problems in the bud. You'll be helping yourself and society and, if any urgent problems do appear, we'll be able to deal with it at the earliest stage possible.

Ted: Um. I *do* like the thought of sharing the information to help others. But I'll have to talk it over with my wife. It will have an impact on her too, you know?

HCP: Of course it will. And if you want to talk to me about it together, then that's no problem at all.

In a third scenario, a young couple could have issues involving their fears about passing on a congenital condition (that they don't know about) to their, as yet, unborn children, but may also want to know what the risks are.

Six Pillars for Policy Makers

It's a fine balance. And, while it's clear that gene sequencing has huge advantages for research and prevention, there can be pitfalls for individuals and their families. In this day and age HCPs need to look at both sides of the coin, as the new science is certainly not going away.

Let's finish by floating the idea that the concept of having full-gene sequencing, and understanding the consequences, should be raised in older school children (in a similar way to sex education) as well as at universities, within HCP training courses (mandatory), and with other stakeholders such as patient groups and even mainstream journalists. For the

broader policy and regulatory communities, the following six pillars need to be taken into account:

1. Standards for data generation and analysis – *Agree on standards for genomic sequencing and analysis*: Genome sequencing has progressed rapidly in clinical and translational research with the development of multiple tools and methods. Defining standards will ensure consistency of clinical testing and also greatly further research by facilitating greater comparability of the increasing number of sequences being performed.
2. Data privacy and sharing – *Agree on standards around the sharing of genomic and associated clinical data*: Genome sequences are by definition personal and have the potential to be identifiable; however, the sharing of data greatly increases the utility of genome sequencing, for example, in confirming the pathogenicity of an identified genetic change and identifying other patients with the same rare disease.
3. Clinical informatics – *Promote the uptake and alignment of existing agreed-on standards and define standards for the interoperability of health informatics systems*: Electronic patient record systems are variably implemented across Europe, but they have few uniform standards and little interoperability. The linking of clinical to genomic data is essential to derive benefit from genomic data, for both health and research purposes.
4. Clinical application – *Coordinate national activity to ensure best practice emerging with regard to clinical implementation and application is shared*: Genomics is starting to be implemented across a number of clinical areas in different geographies. To ensure that models of best practice for clinical implementation and application are shared across these, a coordinating body is required.
5. Clinical education – *Structure a training programme in genomics, informatics and personalised medicine for clinical staff*: The majority of current clinicians have not been trained in the "genomic era" and have little experience with using genetic information in healthcare. For patients to be correctly identified for the most relevant test, and the appropriate information from the results to be conveyed back to them, the general workforce needs specific addressing of this educational deficit.
6. Regulation – *Promote broad discussion with European regulators on the appropriate regulatory mechanism for clinical genomic testing*: Current regulatory mechanisms can make the prompt implementation of effective innovative diagnostics to patients challenging, particularly as genomic tests tend to rapidly evolve and improve after initial release in terms of undergoing frequent hardware, reagent and analysis/interpretation software modifications [2].

Perhaps it's an idea that will catch on, as the gene genie is well and truly out of the bottle.

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