My Cancer & AI

What do cancer patients think about artificial intelligence?

Professor Christopher Yau, **University of Oxford** and **Health Data Research UK**

Dr Charles Gadd, **University of Oxford**

Faye Boswell, **Ovarian Cancer Action**

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Background

My name is **Christopher Yau** and I am Professor of Artificial Intelligence at the **Nuffield Department for Women's & Reproductive Health** at the **University of Oxford**[1] and **Health Data Research UK**.

I am a scientist who specialises in the areas of mathematics and computer science. Specifically, I develop ways of studying health information to understand why people become ill and how we might effectively treat them. I do this by creating computer algorithms that allow us to read and interpret complex sources of information that are often too large to be examined manually.

One of my main areas of interest is **Cancer**.

Cancer

We have never been in a better position to understand why cancers occur and how we might more effectively treat them. The last twenty years has seen the development of numerous technologies that allow us to study cancers in more detail than before. Scientists are now able to routinely probe individual molecules that exist inside cancer cells and to do so with thousands of cells at a time. Remarkably these molecular technologies are now moving from a purely research use and into routine cancer care for patients.

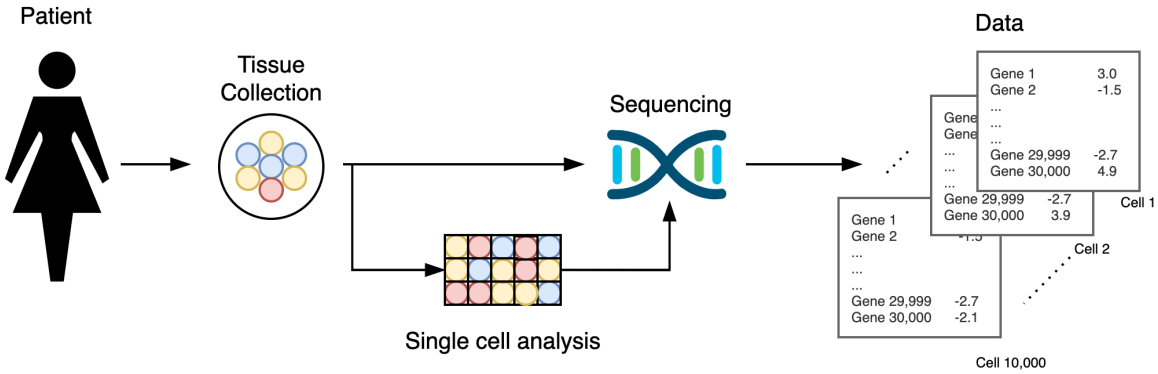


Figure 1: Modern technologies allow us to measure a potentially vast number of molecular properties in cancers. This can result in anywhere from hundreds to billions of pieces of information per experiment.

In the UK, the **Genomics England** 100,000 Genomes Project and now, the **NHS Genomic Medicine Service**, will see NHS cancer patients have access to DNA sequencing. DNA sequencing will allow the unique genetic properties of each person's cancer to be assessed. This can then be used to guide treatments and help patients access clinical trials for novel treatments.

Over the coming years, further molecular technologies will be trialled for cancer care. The information they will provide presents an exciting future for improving outcomes. However, understanding this complex molecular information and the possibilities they yield poses a great challenge for patients and doctors.

How can we help them?

The Fellowship

In 2020, I was one of a number of researchers to receive a **UKRI Turing AI Acceleration Fellowship**. The Fellowship provides funding to relieve me of some of my regular teaching and administrative duties in order to spend more time focusing on research. It also allows me to recruit a small team of researchers to support my efforts. So, what are we proposing to do?

The aim of my Fellowship is to develop computer algorithms that simplify the processing and interpretation of advanced molecular information collected about cancers to make them more accessible to those who need it most (patients and their doctors).

[1] This work was conducted when I was previously at the University of Manchester

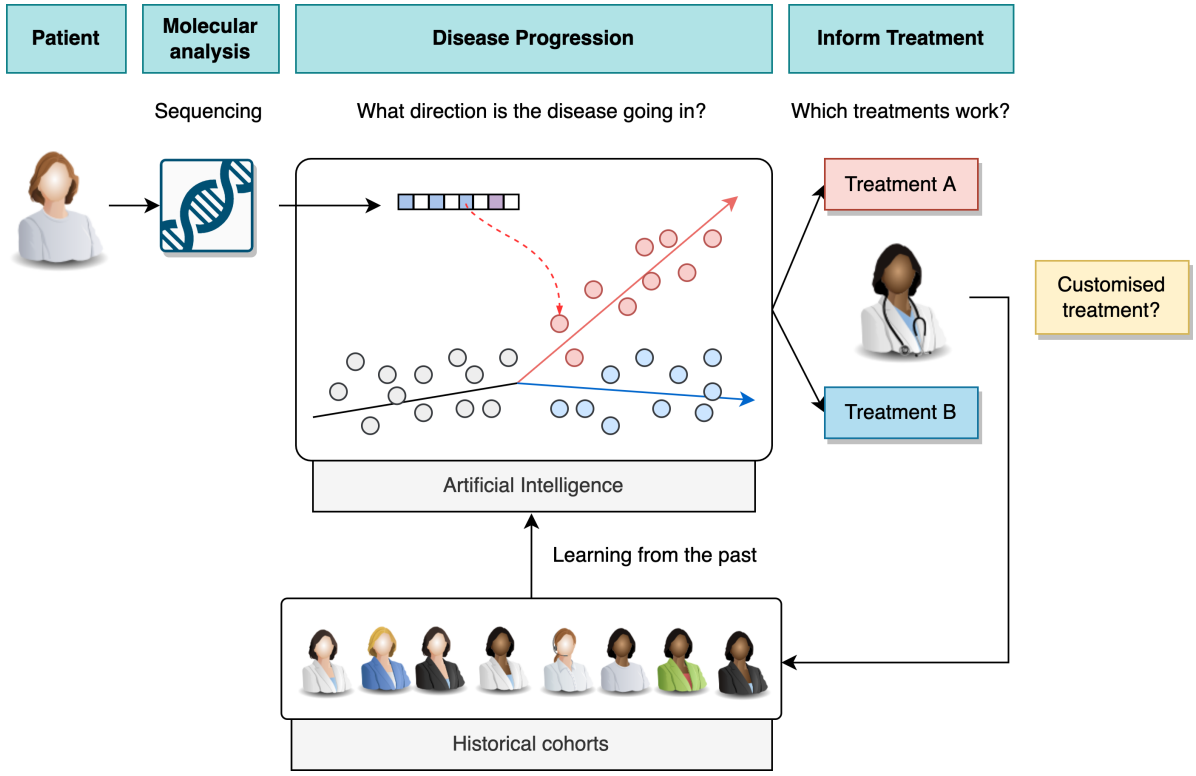


Figure 2: In the future we may see "Learning health systems" in which information about cancer diagnoses and treatment outcomes are used in real-time to update the recommendations for future patients.

Artificial Intelligence

I will use a type of computing technology known as "Artificial Intelligence" or AI. Artificial Intelligence-based systems are designed to "learn" how best to utilise complex information sources to achieve goals that we (as human designers) set for the system. In my Fellowship, I will be designing AI systems that can help us to predict how a cancer might evolve or mutate in the future, how a patient might respond to a particular treatment and ultimately how to recommend the most effective treatment for a given patient and their current state of disease.

There are many advantages to using AI for examining complex DNA sequencing data or other molecules that exist within our cells. First, these data are often so enormous, containing thousands, millions or even billions of measurements that it is not humanly possible to enumerate how all these numbers are connected or should be used. There are too many possibilities to distil this into a set of rules that we manually create ourselves and there is the strongest possibility that our limited capacity for information processing might lead us to contradictory and biased rules. AI systems can automatically construct those rules and, with good and robust design principles in place, can provide some guarantees that the rules will be logical and coherent.

What was the purpose of the workshops?

Artificial Intelligence, like any advanced technology, offers exciting opportunities but also raises issues that require considerable thought for both individuals and society.

One question that I asked myself is "yes, we can do this technologically, but should we do it? What's in it for the patient? What is the collective good?"

Therefore, as part of this Fellowship, I incorporated time and funding to set up a series of workshops with key groups who might be interested in this research. This includes other research scientists, pharmaceutical and other biotechnology companies, clinicians but most importantly, patients themselves.

The workshops were designed to present the work being undertaken, obtain feedback and allow for that

feedback to integrate and modify future research plans. The hope is to truly realise the ambition of genuine patient involvement in research and co-creation.

Why did I want to do this?

My relationship with Cancer is very personal. I come from a family with **Lynch Syndrome** - an inherited genetic disorder that predisposes people to bowel cancer but also to a number of other cancers including ovarian. A number of my family members have been affected by Lynch but I was fortunate to discover that I did not possess the gene mutation that causes Lynch after undergoing genetic testing when I reached adulthood. Nonetheless, knowing that I had the potential to have this condition throughout childhood had a profound effect on my life and professional choices.

It is relatively rare for a researcher such as myself to engage directly with patients about their research. Most tend to leave it to patient-facing clinicians or public and patient engagement specialists. However, given my background, I felt it important to engage directly and actively involve myself in communicating with patients about what I am working on.

How was it organised?

I reached out early to **Ovarian Cancer Action** (OCA) during the development of the Fellowship to set up this aspect of the study. With Faye Boswell, I designed a series that would include three 90-minutes sessions: one for preparation and introduction and two workshops on different research topics. These would be spaced out over a number of weeks held toward the end of 2021. In addition, I would give one webinar to provide a general introduction to artificial intelligence research in cancer. OCA recruited a core group of ten patient volunteers, with experience of ovarian cancer, who are experts by experience, to participate in the workshops and hosted the webinar to its wider supporter base.

What did we discuss?

Each workshop was phrased around a topic and within that three main questions.

Workshop 1: "What can AI tell me that I would want to know? And what might I not want to know?"

The first workshop, entitled "What can AI tell me that I would want to know? And what might I not want to know?" introduced the participants to the technological possibilities I was proposing as part of my fellowship. I presented three scenarios to the patient group. Each scenario covered an aspect of the intended purpose of the research I proposed.

Case study 1: What if artificial intelligence could tell you how your cancer came about?

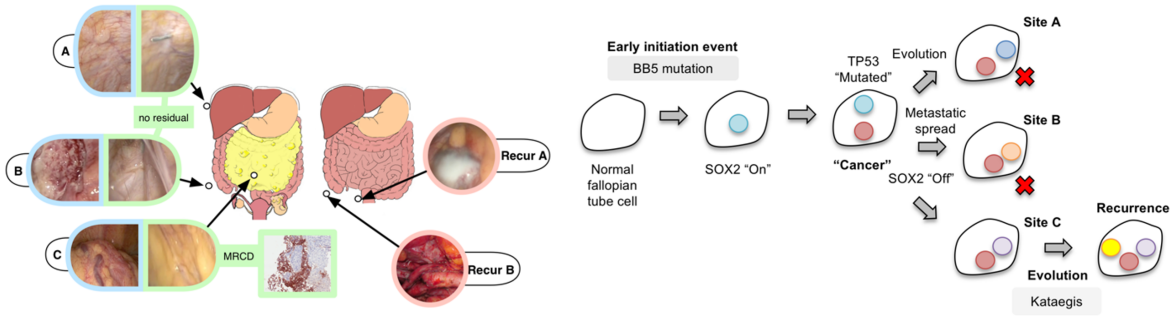
Modern sequencing technology together with artificial intelligence can give us insight into how an individual cancer evolved to the state seen at diagnosis. It can provide patients with a detailed answer to the question of how their cancer arose and what the sequence of molecular events that led to it were.

A significant amount of research effort and work has been undertaken globally in this area, including from my own research group, but a question I have always asked myself is whether this is actually important to patients or merely just interesting scientific curiosity? I therefore asked the patient group the following:

1. Is this information of interest to you?
2. Would it be of more importance if it affected your treatment?
3. What else could this information be useful for?

Within this participant group, it was generally felt that information about how a cancer reached its current stage was not particularly important. Whilst the information was potentially interesting from a curiosity point of view, "I think it is so interesting to see how cells are mutating," remarked one participant, it was felt that "it is important to see how this influences practice" to be of greater importance. Another participant pointed out that for them "at this point, the horse has bolted."

The participant group instead agreed that the information could be useful if it informed treatment with one participant feeling it could be "information to be part of the data my oncologist considers". The group were particularly interested in the possibilities of this information being used for early cancer detection and made "useful for future patients and prevention measures." Participants discussed how "this could be a way forward to getting a screening programme and also giving advice such as the use of HRT and risk of OC". However, there was some caution with one participant making the point that they might not want to know about the history of their cancer if "it showed I had had too much alcohol or the past effects of my hormones."



(a) Multi-region longitudinal tumour sampling

(b) Understanding disease pathogenesis

Figure 3: Combining sequencing technology with Artificial intelligence to allow the molecular history of each cancer to be revealed to the patient.

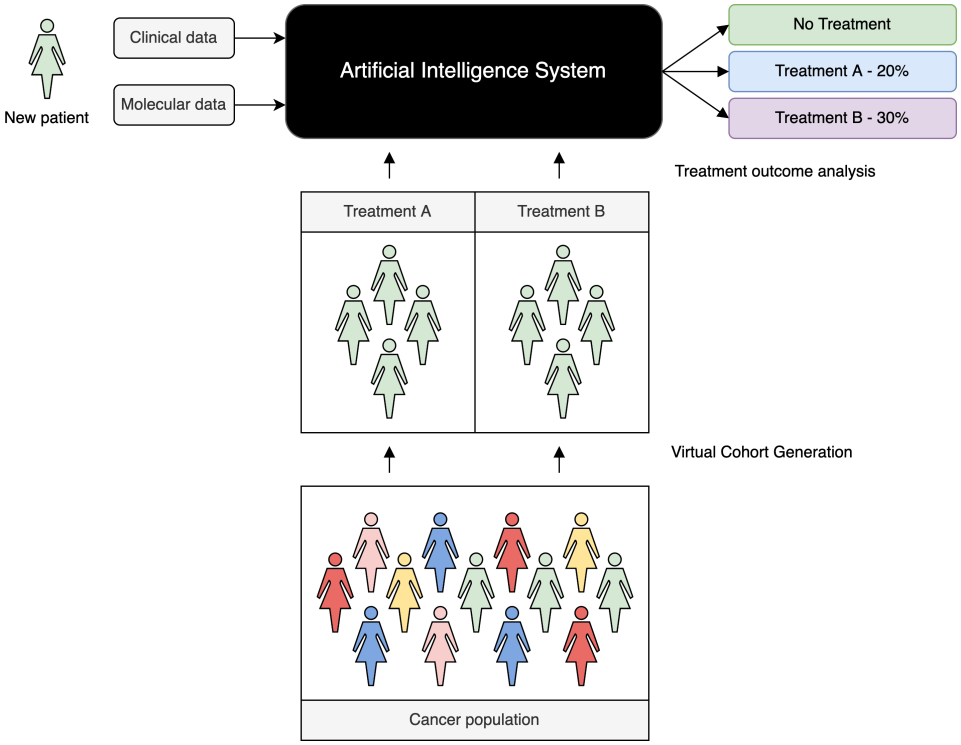


Figure 4: Artificial intelligence use historical cancer data to mimic a "clinical trial" to understand the impact of different treatments on people "similar" to you.

Case study 2: Treatment outcome prediction

We next discussed AI systems that could tell you how successful your treatment would be. I described how AI could be used to produce "virtual clinical trials" using historical data to understand the impact of different treatments on people who are "similar" to you and have been treated in the past in different ways to understand which approach led to the best outcomes. This could lead to personalised treatment plans.

The participant group was then asked if they would trust a treatment recommendation that was derived through this process.

Responses covered a range of opinions. Some participants were encouraged that "oncologists would be basing recommendations through the latest research, and it would give them access to better data and bigger research studies" and supported the principle that "if AI could investigate a treatment plan specific to an individual it would be extremely beneficial." Others were more cautious about the implications of such an approach. Trust was a particular concern with one participant stating that it "would be hard to trust simply because how can you ensure it [the AI system] is trustworthy." Participants described a strong connection to clinicians, with one remarking that "I would inherently trust my oncologist, you are trusting them with your life." Further, another said "I would find it [an AI system] hard to trust, face to face is the best way, I would much prefer a human to a computer." Another participant discussed the developers of AI systems, and who described them as "coder guys in computer science coming up with algorithms, what if they are wrong?"

Questions were also raised about the suitability of the retrospective data that might be available such as "how many individuals would be selected to determine a treatment plan for the patient and how far back would it go?" and what the parameters were for the reach of the system, "would it consider off-label drugs or drugs not approved by NICE? Would lifestyle be considered?"

Case Study 3: Treatment customisation and patient choice

In the third part of the workshop, we asked participants to consider the possibility of using AI technology to give them more say in the design of their treatment and disease management. Predictive AI technology could be used to preview the impact of particular treatment choices and allow patients and clinicians to study different combinations. We posed the following questions about this technology:

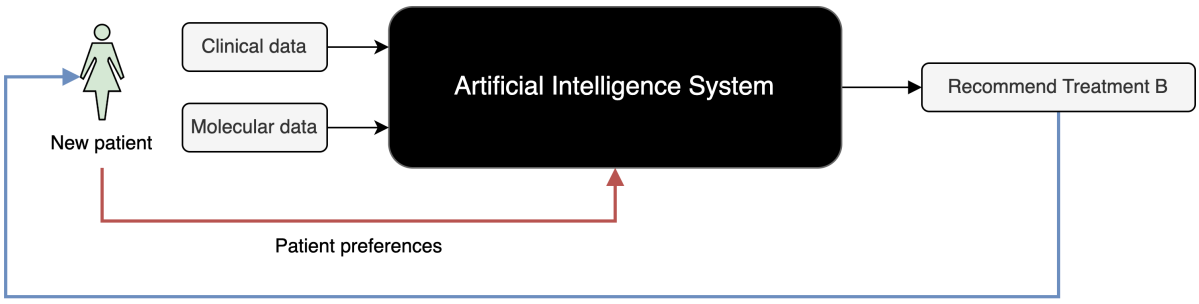


Figure 5: Artificial intelligence could allow patients to "preview" how their choices may affect the outcomes of their treatment.

1. Would you feel more empowered in your conversation with your doctor(s)?
2. Would you feel more confident about managing your choices?
3. Could the option of choice be too overwhelming?

I used a provocative analogy to stimulate discussion by asking if designing your own cancer treatment could become akin to selecting options for a holiday using an online travel booking agent in order to encourage participants to consider the extremes.

This scenario raised several positive responses with one participant remarking that they "feel empowered as information is key, often patients become experts in their own care in long term conditions." Another said that since their cancer was rare, and relatively little is known about it, the choices would help them to feel "like I'm not on my own." Many participants said that they felt confident about being an active participant in decision making though they could understand why some patients would be more reluctant, particularly after their first diagnosis when you can be "a deer in headlights". There was concern about the additional pressure and stress this might place on patients during an already challenging time in their life and some may be unprepared for this. However, this may change over time as the patient learns to live with their condition, suggesting that there could there be different levels of involvement for patients and the need for additional support, e.g. mental health, to enable greater participation.

Participants generally felt that such technology needed to be developed and used in partnership with clinicians and were concerned that this could "potentially mean longer consultations on an already stressed NHS service." It was also important that patients understand any information presented and particularly in "grey areas" (we would examine this further in **Workshop 2**). One participant raised the need for clinicians to be prepared for the types of challenging conversations this technology might enable between patient and doctor and suggested further training in patient interaction.

Workshop 1 Summary and Conclusions

The purpose of the first workshop was to present the patient group with a number of hypothetical scenarios that could be enabled by the proposed research. The group was generally supportive of the proposed innovations but did consider some areas of research to be more of theoretical interest rather than application. What was clear is that the patient group generally showed strong trust in their clinical management teams but that the option to choose to be deeply involved in decision making was important even if it might not always be taken up. It was important that implications of different options would be stated clearly and that the evidence behind such options sufficiently well-developed using appropriate data.

Workshop 2: Risk and uncertainty

Following the first workshop it became apparent that an understanding of the uncertainties involved in decision making would be an interesting topic to pursue with patients. Using the mathematics of probability, many technical experts (myself included) explicitly embed "uncertainty quantification" as part of the development of Artificial Intelligence technologies and point out its importance to potential end-users. However, I have always wondered, would this simply be jargon to patients? And how would a discussion of mathematical uncertainty be viewed from the patient perspective? How would differences in solutions between different device manufacturers be viewed? We therefore set up two case studies to examine these issues.

Case Study 1

We first asked the participants to consider the following statements about an AI-based clinical decision support system. The system can report a measure of uncertainty associated with their output. As a support system, human clinicians make the final judgement about how to utilise the information. In this case, two clinicians draw different conclusions from the same information:

> **Clinician A** uses an AI system to support his decision making. The AI reports that a patient will have side effects with probability 0.1 (10%). The clinician deems this risk low and does not report it to the patient or downplay its significance.
> **Clinician B** uses the same AI system to support his decision making but deems this risk to be sufficient to be worth a discussion with the patient.

We asked the group to consider the following points:

1. Would you want access to uncertainty information?
2. What "threshold" is relevant?
3. What guidance should clinicians receive in the interpretation of AI output?

Many participants articulated that the use of uncertainty information would be dependent on exact context and circumstance such as the severity of the side effects and the degree to which the factors contributing to the information would be comprehensible to them. There was no definite "threshold" of acceptability and "what is acceptable to one person won't be to another patient or clinician."

Participants reported that during their experience of cancer sometimes "side effects were downplayed" and that they "would have expected the clinician to share what to expect with me." The implications of side effects had an impact on their treatment regime, e.g. chemotherapy dosage, with one participant explaining that "some chemotherapy regimens have a higher chance of getting peripheral neuropathy, I wasn't given warning about this so when I got symptoms and reported it the chemotherapy dose was left as it was."

Heterogeneous clinician behaviour was also identified by participants with one remarking "will you ever get clinicians to behave the same way?". Participants generally saw benefits in such systems being made available to clinicians if trained appropriately. It was agreed that clinicians are used to making these decisions based on the information that they have available from diagnostic tools and investigative tests and that these systems would be "... giving them the information in a slightly different way for them to interpret." However, it was cautioned that "everything moves at such a fast pace and clinicians are not always given training on new tools and techniques. In my experience in critical care, you don't always know the extent of their experience." One area highlighted was in the communication of statistical information, where one participant explained that in their opinion, "medics do not have a great understanding of statistics and could improve on their communication skills ... communication skills are important to translate the statistics to the patient."

Case Study 2

The next case study focused on the potential for different AI systems to be available for the same intended purpose. This situation may arise due to different manufacturers producing competing products with different performance characteristics. We wanted to understand how participants reacted to the idea that different medical AI devices might not be aligned in their interpretation given the same evidence. This case study therefore dealt with the higher-level impacts of uncertainty quantification.

Organisation A develops an AI system. Given your information, it reports that your next treatment will be successful with probability 0.8.
Organisation B develops its own AI system, and, given the same information, it reports that your next treatment will be successful with probability 0.6.

We asked the participants about the following:

1. Are potential performance differences between AI products a concern to you?
2. What steps might you hope the health & social care system takes to select the "best" product?

The example provoked a strong response from one participant, "For a patient, the difference between 0.8 and 0.6 is massive, it makes me shudder and the impact on the patient would be huge." Participants discussed the trustworthiness of the manufacturers and the reliability of the data that informed their products. There was some scepticism about whether market competition would enable the most effective solutions for patients and the common good and that more effective collaboration between commercial organisations should be encouraged. Appropriate regulation was also discussed and the importance of having a credible patient voice in the development of any oversight. Participants suggested that more openness and collaboration by health and social care organisations would be beneficial and highlighted the impact of COVID on overcoming traditional barriers to data sharing.

Workshop 2 Summary and Conclusions

The purpose of the second workshop was to present the patient group with a couple of scenarios in which interpretation of risk and uncertainty might be required by patients. The group highlighted challenges in this area and that consideration of various forms of uncertainties could be overwhelming for patients. Accurate communication was vital as well as education of key stakeholders. Collaboration between different parts of the health and social care sector was also highlighted as necessary to put patient needs at the centre of innovation and to reduce variability in technological solutions that might add to patient confusion.

What did I learn?

I have previously given many talks to patient and public groups about my research, but these were largely one-way interactions in which I explained my science. This was an opportunity for a two-way engagement that would lead to potential changes in my research direction.

These workshops tested fundamental assumptions underlying my research and I learnt that there were a heterogeneous range of thoughts and opinions about these assumptions. The technology I planned to develop would give patients more information about their cancer but the use and communication of this information needs to be carefully considered and may need to be adopted suitably on an individual case-by-case basis. There is huge trust in clinicians by patients but also concerns about whether clinicians will be appropriately trained to handle new data and technologies.

Throughout the workshops, what I can describe as "information overload" was an implicit concern, particularly at a time when patients would be at a vulnerable stage of their life. A difficult balance must be struck between simplicity of presentation and communication but also each patient's need to receive accurate and informative insights about their condition and how this should be used to frame potential choices and decision making. Using AI to empower patients is something I wanted to do but there is far more to it than I first envisioned, and this workshop brought up various dimensions I did not consider.

How has this affected my research?

After these workshops, I have given specific thoughts to changes in my research plans. The key changes have been in prioritisation. Previously I had proposed a lot of work looking at cancer evolution, but this aspect of my research has now been reduced and we will be focusing more on prediction and what is most important for treatment planning. For example, in our work on how chromosomal abnormalities arise in cancers, instead of focusing on how they came about, and the processes involved, we are now examining what those abnormalities mean for prognosis and treatment outcomes.

I am also devoting more of my own time and those of my research team to communicating their work more widely, particularly to clinical collaborators, to better understand how we can go about more effectively communicating our research because educating others in these new ideas. This will be a bit of a trial-and-error process as we work out the best approach to take. It will also be of particular interest to see how I adapt approaches to engage with industry partners to ensure patient experiences are central to discussions within partnerships that are also developing as part of my fellowship.

Will I do this again? What comes next?

I plan to develop more workshops in the future. As our research progresses and we begin to develop prototypes of our technology, I would like to get feedback from patients when presented with these mock-ups. It is vital for the success of this research that these technologies be useful, and the outcome of these workshops has been to tell me that while clever mathematics clearly underpins technological development, usefulness is based on acceptability of the technology by its end-users. I hope that by involving patients throughout this research we can create innovative and useful technologies for cancer.