The Terry Fox Research Institute’s West Coast Dialogue: are we prepared for personalized medicine?

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ABSTRACT

This meeting report is the second in a series by the Terry Fox Research Institute about its Pan-Canadian Dialogue Series on Cancer: Let’s Get Personal, a public research and outreach project. The inaugural dialogue was held in St. John’s, Newfoundland and Labrador, in April 2010 on the thirtieth anniversary of the Marathon of Hope. That dialogue launched a continuing conversation that the Institute is having with the Canadian public during 2010. This report summarizes the dialogue held at Simon Fraser University’s Morris J. Wosk Centre for Dialogue in Vancouver, May 12, 2010: “Are We Prepared for Personalized Medicine?”

The world is in the midst of a technology renaissance that will change medical practices and improve cancer treatment for every individual. Do we know how society will be affected by personalized medicine over the coming decades? Members of the medical and scientific communities in British Columbia and the public, including cancer survivors, patients, and caregivers, discussed the challenges that lie ahead for Canadians—ethically, economically, socially, clinically, and from a health management perspective—in preparing for personalized medicine, which some experts predict to be fewer than five years away. New technology, including advances in DNA sequencing, will require tough choices and decisions to be made by society, and values will be at the centre of those decisions. The directions taken will change health care as we know it today. Issues such as societal values, freedom of information, access, consent, and having personal genomic information literally at our fingertips will form the heart of the discussion.

KEY WORDS

Patient-centred care, personalized medicine, cancer, genetics, genomics, health system, prevention, freedom of information, access, consent

1. INTRODUCTION

This meeting report is the second in a series by the Terry Fox Research Institute (TFRI) about its Pan-Canadian Dialogue Series on Cancer: Let’s Get Personal, a public research and outreach project. The inaugural dialogue was held in St. John’s, Newfoundland and Labrador, in April 2010 on the thirtieth anniversary of the Marathon of Hope. That dialogue launched a continuing conversation that the Institute is having with the Canadian public during 2010.

The present report summarizes the dialogue held in Vancouver, May 12, 2010, at Simon Fraser University’s Morris J. Wosk Centre for Dialogue. With help from medical and scientific discussants and subject-matter experts in oncology, genomics, ethics, and economics, the West Coast Dialogue focused on the challenges that lie ahead ethically, economically, socially, clinically, and from a health system management perspective as we embrace the new reality of personalized medicine.

Terry ran one mile at a time. He was driven to discover what lay beyond the next corner or crest of a hill. With every step forward, he was one step closer to completing his journey. I see similarities to why we are gathered here tonight. Gathered in this room are researchers, clinicians, health care professionals, caregivers, survivors, supporters, and the public. We will not solve the cancer problem tonight ... but through dialogue and collaboration we will take another step forward.

— Darrell Fox (Terry Fox’s younger brother)
2. THE CHALLENGES OF PERSONALIZED MEDICINE

2.1 A Technology Renaissance

Two scenarios presented in Vancouver helped to crystallize what the future will look like as recent and rapid technologic and scientific advances catapult humanity into the world of personalized medicine:

- In the one instance, an expert in applied genomics wondered aloud, “If someone has a tumor, and we sequence that tumor to identify which treatment they should be using, embedded within that data will be their susceptibility to many different diseases. Who will impart that information? You can’t just say, ‘Here is your genome ... go home and look at it.’ This is incredibly personal and important information that can be misinterpreted. We don’t have a health care community who are equipped to deal with it.”
- In the other instance, a radiation and a medical oncologist envisioned a personal ad in the world of real-time gene sequencing: “Single, attractive, fun-loving male seeks life partner. Send complete gene sequence, photo optional. No mutations only, please.”

These two scenarios point to a future significantly altered by new technology—the DNA sequencing of the human genome and of diseases such as cancer—and the perhaps cataclysmic change that this technology may bring into human life, society, and the health care system if proper preparations are not made. The scenarios also identify the challenges that have to be faced in preparing for the new reality, which some experts predict to be fewer than five years away.

But do we truly understand how personalized medicine will affect us over the next decade?

The words “personalized medicine” are used often in cancer care and research conversations, often describing a common goal of providing the right treatment for the right person at the right time.

Personalized medicine is going to change our future. It will change the way we practise medicine and how we think about health. Can we actually conceptualize and think about what the future might look like in terms of personalized medicine, and can we prepare for it?

With the new technology, scientists and medical practitioners can characterize cancer so much better than was previously possible. “So instead of seeing 200 people with the same disease, we now see 10, 20 diseases. And I suspect, in the next few years, what we’ll find is that every single person has an individual type of cancer. It’s only a matter of developing the technology that will allow us to see that,” said hematologist and dialogue co-chair Dr. Clay Smith (BC Cancer Agency), setting the stage for the evening’s discussion.

Co-chair Dr. Simon Sutcliffe, senior advisor at TFRl, provided a brief historical view of how the computer and information ages have transformed the world since the 1960s: “In 50 years, a technology transitioned from business and commerce to social, day-to-day networking. The image on the left [see Figure 1] shows 92 gene sequencers ... The image on the right shows one bench-top sequencer. Remarkably, only four years have elapsed between the two images. What four years ago roomfuls of equipment used to do is now replaced by a single piece of equipment sitting in one room. This is giving us real-time, real-world sequencing to apply real-world decision-making in the relevant timeframe of the patient and the relevant cost of the health care system.”

Sutcliffe’s “personals ad” analogy described earlier portrays how DNA sequencing technology may transform our world in a very short time. It also underscores the need to address the challenges that come with a technological transformation that will enable each and every person potentially to carry around their DNA sequence, if not in a back pocket, then perhaps on an iPod.

The technology has been advancing extremely rapidly, explained Dr. Robert Holt, senior scientist at the Genome Sciences Centre, BC Cancer Agency, and co-director for the Genome Canada/Genome BC genomics platform. In 2002, when the first draft genome sequences for a human being were completed, the cost had been probably several billion dollars. “It’s come down now to a few thousand dollars. Now, it costs about ten thousand dollars, and it takes about three or four weeks to sequence a genome. But it’s changing quickly.”

Disruptive “next generation” sequencing technology

The diagram illustrates the rapid decrease in cost per base, with an increase in throughput per instrument per year. The figure shows the transition from the Old Generation technology, which required 92 machine-years to sequence a genome, to the New Generation technology, which can sequence a genome in 1 machine-week.

*Figure 1* Sequencing technology. Image provided by the BC Cancer Agency, Vancouver, BC.
And so is our understanding of cancer and how to treat it: “We’re starting to treat tumours not by where they occur (which is what we have been doing for the past two thousand years), but by what they are.... It’s a huge change,” remarked Dr. David Huntsman, medical director of the Centre for Translational and Applied Genomics at the BC Cancer Agency and a professor of pathology and laboratory medicine at the University of British Columbia.

Personalized medicine is essentially going to be about what we can afford, what we're prepared to prioritize, what we're prepared to give up, and how, individually and collectively, we prioritize the importance of personalized medicine in our decision-making.

Sutcliffe provided the audience with the fictitious case of a person aged 50–60 years who is diagnosed with colon cancer, comparing what would have been done 25 years ago with current-day treatment, and projecting what care for a similar case will look like in 20 years: “We [will] still recognize that disease progression is a clear risk. A number of new technologies will allow us to distinguish with a fair degree of confidence who actually doesn’t need any further treatment and who does require treatment. For those who do ... there will be a range of options that can be selected according to tumour characteristics including molecular profile and patient preferences. The treatment will be relatively brief, probably three months. And should the disease progress, there will be a number of options that can be pursued to control it.”

The difference over 50 years is that the therapies will lead to distinct improvement, predict who will do well with a particular treatment, and determine the treatment or treatments that will be best for the patient.

Oncologists will draw from a palette offering greater versatility because of advances in genome sequencing and new technologies that will create molecular profiles and biomarkers, establish new treatments, and target individual cancers.

Twenty years ago, we “lumped” everything together. Today, we “stratify” by aggregated characteristics. Tomorrow, we will individualize and personalize.

2.2 Ethical Issues and Societal Values

Real-world gene sequencing is blazing a path toward personalized medicine, but are we prepared for the huge questions and decisions that tag along? Much needs to be considered—ethical, economic, clinical, and systems management perspectives—and our individual and collective values are what lie at the heart of this matter.

Health ethicist Dr. Michael McDonald, Maurice Young Chair of Applied Ethics at the University of British Columbia, framed the ethical discussion for participants with myriad questions relating to how impending scientific changes will affect our future and that of our children:

- Our pursuit of personalized medicine means that we will have to give up some other things. What are we giving up? Who wins and who loses if we invest in personalized medicine?
- Will we address the needs of the most vulnerable in society? Is the pursuit of personalized medicine providing more for the most privileged parts of society at the expense of those worse off?
- As we become more excited about personalized medicine, will it move us away from attention to the moral and social challenges posed by poverty, inequity, and lack of access to the essentials of life?
- Who will have access to personalized medicine? How? Will it drive health care costs up or down?
- Will we start to think of ourselves as an assembly of genes? If so, will we then miss some of the vital environmental and cultural influences that make us who we are?

For one speaker, the term “personalized medicine” is a misnomer. Robert Holt alluded to the duplicity of the term: “I was asking my son, who is 15, ‘What do you think personalized medicine means?’ ‘I guess designing drugs for one person,’ he replied. ‘Do you see a problem with that?’ I asked. He replied, ‘Yeah. What about the other six billion people?’ Personalized medicine cannot mean drug design in a boutique way for an individual—there's absolutely no equity in that proposal.”

The ability to characterize a person’s genome and to identify whether that person will develop cancer or whether a particular treatment or drug will be effective and tolerated are some of the advantages that this technology will soon provide. On the other hand, accurately predicting a patient’s response based on a given genome sequence is not particularly meaningful if alternative drugs cannot be provided. Many oncology drugs have no (current) alternatives. The technology comes with limitations.

Many questions are still in need of answers and solutions. The importance of societal values and of the public having a say in how personalized medicine unfolds was emphasized by many participants.

“We know that the public likes researchers, clinicians, and other health professionals to make certain technical judgments when it comes to health care. But we also know that the public wants a place at the table when we are discussing the values that underpin health services. Values are central to any health system.... As an economist who works very closely with ethicists, I am interested in knowing...
what the values of the community are, because it is those values—and you as citizens—that should drive the health system," remarked health economist Dr. Stuart Peacock, co-director of the Canadian Centre for Applied Research in Cancer Control and a senior scientist at the BC Cancer Agency.

“No group of clinicians, researchers or public policy experts ... can sit together in a room and come up with the solutions for how to do this,” said David Huntsman. “Large-scale community engagement [will be necessary] because it’s a complete paradigm change in the way we practice disease control medicine.... I would see this as Day One in community engagement, because if we are going to control cancer in a 20–20 fashion by the year 2020, we are all going to have to work together to get there.”

2.3 The Economic Issues

How much will it cost? What can we afford? What can we not afford? Who will pay? Those questions and their answers are important in any discussion of personalized medicine. Peacock said that his mind is occupied most of the time with two questions:

- How can the health system be made sustainable?
- How can it be made fair?

The question that must be asked, he said, is do we want a health system based on ability to pay or do we want it to be free at the point of use as is currently the case [in BC and Canada]? “Put that into the context of rising drug prices and a very weak economy (at least for the foreseeable future). Can we actually afford to continue to go along the trajectory we are on at present? Is the current health system model in B.C. sustainable?” asked Peacock. “I would suggest to you that we need to plan for the possibility that the health system as we know it is not sustainable. And, given that, we need to think very carefully about how we move forward.”

“What can we expect from government?” asked an audience member. Will the country or the province subsidize personalized medicine—particularly for people who do not have the money to pay for it?

“This [subsidization] is a question that virtually every developed country is grappling with at the moment. If you look at the example of New Zealand, they are doing something around what they call ‘core services.’ They are trying to identify which health care interventions the government will subsidize and which ones they won’t. They’ve tried this once before, and it’s a very difficult task. So the answer is [that] we don’t know how expensive these treatments are going to be. We do know that health care costs—inflation, drug costs—are going up substantially over time. Between ten and twenty per cent each year,” said Peacock.

With health care constituting the largest sector of the economy for most developed countries, governments are grappling with these issues. A reasonably conservative view is that some very difficult choices lie ahead for communities and for governments. The United Kingdom and Oregon are two jurisdictions that have involved the public in discussions with government about making hard choices.

Some suggested that more resources be allocated to prevention to reduce system costs. “We have the technology today called ‘colonoscopy’ that, if we had the political will and economic resource to provide to every individual at age 50, we would prevent invasive colon cancer from happening and people from dying from that cancer. I’m hoping that we can apply even low-tech technologies in the future so that personalized care can include a very strong dose of prevention,” commented Dr. Doug Horsman, retired pathologist and geneticist (BC Cancer Agency).

Prevention also figures into the cost equation in other ways: “When you think about how we treat lung cancer, we spend an enormous amount treating late-stage lung cancer when a person is going to die. We could redirect those resources into prevention earlier on to prevent [the person] from getting there in the first place,” said Peacock. When students asked him about the most cost-effective treatment or intervention that he is aware of and that is not being sufficiently exploited, he mentions general practitioners providing advice about how to stop smoking. “Why aren’t we doing more of it?”

2.4 System Preparedness for Change

2.4.1 Sustainability, Affordability, and Accessibility

Can we take this high-tech approach to cancer care and roll it out in an equitable and fair fashion across society? Can we ensure that personalized medicine does not mean creating some incredibly specialized new test that benefits only a small number of people?

New treatments are expected to yield cost savings as well as provide more effective results: “By increasing response rates and efficacy ... we’re saving costs as well. It is yet to be determined what the net cost [of personalized medicine] will be, but it will probably be higher. There is enormous opportunity for cost savings,” remarked McDonald.

He described the potential for vaccinations (at a population-health level) to prevent cancer, referring to the new vaccine Gardasil (Merck and Co., Whitehouse Station, NJ, U.S.A.), used to prevent cervical cancer caused by the human papilloma virus. “The new sequencing technology allows us to sequence and probe with much greater sensitivity for the presence of infectious agents in cancer, novel ones that can be the basis for new preventive vaccination strategies.”

Dr. Jerome Yates, a member of TRI’s scientific advisory board and national vice-president emeritus for research for the American Cancer Society, advised that the health system will have to make social changes and invest more into behavioural research to ensure that primary care is implemented on an individual basis.
“We need to think about how the system is going to need more health educators—for the very reasons you alluded to in terms of the Internet and the availability of information, much of which, by the way, is false when the patients bring it in to their physicians. So it has to be triaged,” he said. “We need to [pay] more attention to what we can do to change behaviours of the providers as well as the patients.”

“I think we have a very large balancing act to do in making sure we are embracing the new technologies, and certainly moving some of those forward and at the same time investing the dollars in prevention,” remarked Cathy Adair, Vice-President, Cancer Control, Canadian Cancer Society (BC). She mentioned the need to invest in poverty and education—social determinants of health—and in non-traditional health care areas.

Population health expert Richard Gallagher, Cancer Control Research Program, BC Cancer Agency, described the differences between primary and secondary prevention. The former looks for factors that cause cancer and tries to intervene by preventing exposure to those factors; the latter involves using known technologies to try to intercept the disease process at the earliest possible time. “We are at the start of a major—in fact, the biggest—[primary] cancer prevention exercise in the history of Canada, recruiting 300,000 Canadians ages 35–69 into a large prospective cohort study to investigate the causes of cancer. Not only common things like smoking and diet, but also looking for environmental causes.” That program is sponsored by the Canadian Partnership Against Cancer.

One of the problems Dr. Pippa Hawley (BC Cancer Agency) sees is that currently available drugs are not being used effectively. She leads the Agency’s Pain and Symptom Management Palliative Care Program. “[Take,] for example, simple access to opioid-type pain medications for cancer patients. Whether they’re either cured of their cancer or undergoing treatment, there is still very poor access to these drugs that are available. System-type research to make sure people get access is something I think gets neglected.”

2.4.2 Privacy, Consent, and Freedom of Information
Issues relating to privacy, consent, and freedom of information must also be addressed, say the experts. “If we are going to capitalize on this future, we need to be thinking about the nature of informed consent: what we consent to, and for how long we consent,” remarked Sutcliffe. These discussions will require us to consider current language, acts, and policies that govern these areas and to work collaboratively with regulatory agencies that have oversight over these rights.

“We have to ask about impacts on privacy as researchers access patient data,” commented McDonald. “To what extent does this change our attitude toward what is personal and what is impersonal?”

“Will people, once they know all this data, be subject to genetic discrimination? What is someone going to do if they have the knowledge that they have a genetic predisposition? People are already confronted with this. Now we may all have some information. What are we going to do with that in terms of our own lives?” asked Smith.

2.4.3 Managing Information and Health Care Resources
These new kinds of technologies will generate huge amounts of data—log orders beyond what we are used to, remarked one researcher. “We can barely manage the kind of data we have right now. What will we do when confronted with a hundred or a thousand times more data on individuals?”

And then there are the issues of the costs associated with storing and interpreting this data. “DNA sequence data isn’t one hundred per cent accurate. We get around that now by sequencing to a certain depth to overcome [the need for] multiple sequencing, which adds to the cost,” remarked Holt.

One participant wondered about the effect of having this information at one’s fingertips. How is the information to be shared with patients? How is the acquired data to be managed? What will it be like for people to look at their genes and have someone say, “This is what your future looks like this many years down the road”? We may have the drugs to manipulate or change a gene, but we also may not. How do people go through life knowing that?

“When we move to testing for susceptibility to diseases lots of engagement has to go on. People have to understand the risks and benefits of testing. But if someone has a tumour, and we sequence that tumour, we don’t have a health care community that is equipped to deal with imparting the information to the patient. But we need one, because people are going to start visiting their doctor and saying, ‘I know I have a migraine, but I have my genome on my iPod. How does that affect how you are going to treat me?’ Our hand is going to be forced here; we have to really change the way we think about disease control; how we interact with patients; how we use Web-based educational tools,” said Huntsman. It will take a new breed of health care professional who can use this information.

McDonald further posited that people are going to be accessing health care in highly unconventional ways—for example, using mail-order kits or the Internet—that will intersect with conventional health care delivery. “This technology and its availability is going to explode way outside our conventional system, and it’s going to make a political difference and a social difference.”

2.4.4 Treating the Whole Patient
People also need to think about what health care will look like in the future. How will patients actually be treated as persons? What are their needs beyond their genes and their molecular targets? How is patient-centred care defined? What are the individual’s priorities, and will the medical system be responsive to those priorities over and above the relevant bio-medicine?
Those were among the questions raised by Sutcliffe in his presentation about “system readiness” for change.

Several attendees said that there is more to health care than treating a patient’s tumour or knowing his or her DNA sequence. Care is about treating the whole person in an integrated way.

“What are the other things on a personalized level that we can do for [a] patient from a whole-person perspective? Can we empower the patient to take responsibility for their health, to actually do something for themselves rather than just accepting an expert opinion and the treatments given to them? On a personalized level, too, patients need different information and make different choices and decisions based on their backgrounds, their culture, or whatever,” remarked Julius Halaschek-Wiener, director of research for Inspire Health, an integrated cancer care clinic in Vancouver.

In terms of personalized medicine, other patient needs may require attention: emotional aspects, issues of empowerment, and other matters that go beyond a patient’s genetic sequence and the characterization of a cancer.

3. SUMMARY

Implementing personalized medicine is not a political, medical, or patient decision. No single constituency will put it into place. Doing it—and doing it efficiently and effectively—will require the involvement of multiple constituencies providing various kinds of input. Society will be influenced by the actions of others: for example, our U.S. neighbours and other research and development competitors, including evolving markets such as China and India.

Says Sutcliffe, “What medicine can do is provide the scientific and technical answer. It can talk about effectiveness. It can talk about costs. It can talk about cost-effectiveness, and it can rate things against each other. For example, X would be more cost-effective for a certain endpoint than something else. The real challenge is [the value that] is actually attached to that scientific and technical piece of work. The government won’t attach a value to it unless there is a public value that causes the government to think about it in a certain way.... The decision will come about because evidence-based information is put in the context of value, value is expressed as a priority, and action would be taken on a priority.”

“Hope for the best: We have lots of new personalized medicines that do, and will, provide great benefits to patients. Plan for the worst: These new therapies are going to be tremendously expensive,” advised Peacock.

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The point was made that we can’t have it all. There will be questions about winners and losers, [about] how we try to ensure that genetics/molecular medicine is a “force for good” and a means of providing better individual and societal outcomes, rather than a “force” for inequity, discrimination, individual and societal injustice.

—Mr. Tony Penikett, moderator and adjunct professor, Master of Public Policy Program at Simon Fraser University

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“Our intent was to stimulate discussion around a few questions. Why do we want personalized medicine? Do we want it at all? To me, it makes sense as an approach to improving outcomes, decreasing side effects, and hopefully, providing a better chance for people either to not get cancer or, if they get cancer, to do better once they have it,” remarked Smith.

Final remarks from Dr. Victor Ling, tFRI president and scientific director, reflected the feedback of many participants: “I hadn’t realized how big and complex an issue this is. In many ways, we are like the proverbial blind men trying to understand what an elephant is all about.”

There will be important decisions to make in the next few years. Humanity is at a crossroads in cancer care and research today. The future is around the corner, and everyone needs to prepare for it.

Personalized medicine will move us closer to the goal of improving outcomes for cancer patients. Terry Fox’s remarks from 30 years ago clearly remind us today why we must never lose sight of the goal of a world that is cancer-free:

As I went through the 16 months of the physically and emotionally draining ordeal of chemotherapy, I was rudely awakened by the feeling that surrounded me throughout the cancer clinic. There were faces with the brave smiles, and the ones who had given up smiling. There were feelings of hopeful denial and feelings of despair. My quest would not be a selfish one. I could not leave knowing these faces and feelings would still exist, even though I would be set free from mine. Somewhere the hurting must stop, and I was willing to take myself to the limit for this cause.

To view the complete remarks of the session leads and panellists, please visit www.tfri.ca/dialogues.

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