Ten years of BRCA testing: comparing experiences from an international perspective

Report of CSG/CGC workshop
Utrecht, 24 April 2006

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The first half of the 1990's was an exciting period in the emerging field of cancer genetics. In these years susceptibility genes were identified for both colon and breastcancer. The knowledge of these genes opened up new possibilities for identification of individuals at risk for hereditary forms of cancer. BRCA testing became one of the first much debated examples of more large-scale DNA testing relating to a common disease in the (female) population. Today, in 2006, we may look back on ten years of BRCA testing. It is very interesting of course to see what we have learned from these experiences about the challenging and controversial questions that were raised about the prospect of BRCA testing ten years ago. In a workshop organised by the *Centre for Society of Genomics* and the *Cancer Genomics Centre* in April 2006 three speakers discussed their visions of these experiences from an international perspective. Participants in the workshop represented a broad scientific interest in the field of BRCA testing.

Since breast cancer is the most frequent cause of cancer deaths among women, and 5 to 10 % is commonly attributed to inheritance, hereditary breast cancer is considered as one of most common genetic diseases in the industrialized world. In this context, the isolated BRCA genes have been welcomed at the time as the first genes for which wide-spread presymptomatic testing might be appropriate. Indeed, with the introduction of BRCA testing, clinical genetic care was going to expand from a relatively small number of families who had already been identified as being at risk, to potentially large numbers of individuals with no prior knowledge of their risk status. This prospect aroused a variety of challenging and controversial questions.

- Who should be offered a genetic test identifying BRCA mutations? Only those individuals with a clear family history of breast cancer, or also those without a significant family history?
- What kind of information was there to offer to those receiving a positive test result about life time cancer risks and what options were available to these individuals for screening and prevention?
- What would be the psycho-social impact of BRCA testing, especially when testing would be extended more and more to individuals beyond established risk groups?
- What would be the implications of more widespread practices of BRCA testing for the organisation of health care, what should be the role of various health care professionals in these new practices of BRCA testing?

These questions reflected a tension between quickly rising expectations on the one hand and a lack of long term practical experience on the other. How have answers to these various questions been sought and found in the past ten years of BRCA testing? This theme was taken

up by a special guest and first speaker in the workshop, Shobita Parthasarathy (University of Michigan, US), who recently finished a comprehensive comparative study of the history of BRCA testing. In her study Parthasarathy contrasts the very different ways in which the international developments in the BRCA research field have been taken up in the two different health care systems of the United States and Brittain. Thus she shows that national context plays a very important role in the ways practices of BRCA testing have been built. In the United States, BRCA testing has been built as a commercial laboratory technology that is available on demand, while in Brittain, it is a clinical service offered by the government's National Health Service only to those deemed to be at 'high risk'.

In her presentation Shobita Parthasarathy argued that these different systems of BRCA testing also embody different definitions of users and different understandings of risk and disease. In the American system, tests can be ordered from Myriad Genetics as a commercial provider through any physician, and specialised genetic counseling is not required. In this context, women with an interest in a BRCA test may be considered as *consumers* who have almost unlimited access to the system by seeking out the help of a physician who is willing to facilitate the process. Services however often will (have to) be paid out of pocket. In the British system, on the other hand, equal access is an important goal and is bolstered by the gatekeeping authority of health care professionals. In this context, BRCA tests are offered only to women who are defined as high risk on the basis of family history. Thus, women cannot demand access to specific services, but as a *citizen* and *patient* have the right to be referred to the system on the basis of medically established clinical need. The different approaches in the American and British system also entail, as Shobita Parthasarathy pointed out, different definitions of risk and disease. Whereas the American system focuses on the identification of BRCA mutations as a distinctive symptom of *hereditary disease*, the British approach emphasizes *family history* and uses BRCA testing only as a tool to refine a high risk category within a larger population 'at risk'.

Dutch researchers have also been very active and visible in the international BRCA research field and on the basis of this involvement BRCA tests have been readily introduced in Dutch clinical practice. The experiences in the Netherlands were discussed in this workshop by two speakers. Hanne Meijers (Erasmus Medical Centre Rotterdam) explained the way in which practices of BRCA testing in the Netherlands have developed and how women respond to it. In the context of the public health care system of the Netherlands, the Dutch approach has been shaped in a way that on many points is similar to the British system. Women may get access to a BRCA test on the basis of family history and testing is provided in the context of specialized services of counseling, monitoring and prevention. A significant aspect of these services is that, if a woman at high risk wants to be tested, a family member who has been affected by breast or ovarian cancer has to be tested first in order to optimize the chance that a relevant mutation will be found.

This latter aspect returned as an important point of concern in the presentation of the third speaker, Marianne Boenink (Department of Philosophy, University of Twente), who studied the personal experiences of women applying for a BRCA test in a Dutch Centre for Clinical Genetics. As Marianne Boenink emphasized, women who want to have themselves tested have to deal with a lengthy and complex trajectory. A most important, and for many women also unexpected, issue in this trajectory is the active input that is required from individual clients in gathering data on their family history. In order to establish a client's risk status and to decide whether testing might be appropriate, information about the history of disease and causes of death in different generations of family members is required. A client who does not have all the relevant information will be advised to inquire with their relatives. To many women, according to Boenink's observations, it is this aspect of the trajectory that appears to be most burdensome. This also holds of course for the next step in this trajectory, when women have to approach family members who have been affected by the disease and ask them whether they are willing to have themselves tested.

Another point Marianne Boenink raised is that even when women go through all the effort needed to find out their individual risk status, the BRCA test result often will remain ambiguous. According to current estimates, BRCA mutations will be found in 25% of the families with a pattern of disease suggesting hereditary breast/ovarian cancer. Thus, when relevant family members test negative and no mutation is being found, there remains a conflict between the test result and estimations of risk based on family history. In those cases indeed, the final test result is considered only of limited relevance for decisions about monitoring and prevention. In other words, while the burden of BRCA testing is substantial to women, for most of them the benefit is but slight.

It is interesting to compare these Dutch experiences and perspectives to the foregoing observations about the American and British systems of BRCA testing. In her presentation Shobita Parthasarathy emphasized how clients in these systems are being defined in different terms, that is, either as consumers or as citizens and patients. What the Dutch experiences suggest is that another distinction in regard to the clients of these systems may be equally important. Whereas in the American system women are defined as *individual* clients who may seek test information on their own, in the Dutch and British situation the client is primarily defined as member of a *family*. Marianne Boenink's presentation was especially revealing in this respect, because it made very clear that the roles, obligations and responsibilities that are implied in this latter definition, are felt as a real burden by women applying for a test.

In this light the question was raised, during the discussion following the three presentations, whether we should not think more seriously and favourably about approaches that may spare women difficult journeys through the family. Comparing experiences from an international perspective thus invited the participants in this workshop to reflect on the merits of different systems of BRCA testing. In this way it also became apparent that ethics is at issue, not only in discussions about practices of individual counseling and decision-making, but also when thinking about the 'architecture' of systems as a whole.

Further reading:

Shobita Parthasarathy, Architectures of genetic medicine: comparing genetic testing for breast cancer in the USA and the UK, *Social Studies of Science 35 (1),* 2005: 5-40 (a more comprehensive study will be published by MIT press in 2007: *Building genetic medicine: technology, disease, and the national politics of health care*).

Marianne Boenink, Genetic diagnostics for hereditary breast cancer. Displacement of uncertainty and responsibility, in: G.H. de Vries & K. Horstman (eds), *Genetics from the laboratory to society*, Palgraves 2006 (also published in Dutch: Genetische diagnostiek voor erfelijke borstkanker, in: *Genetica van laboratorium naar samenleving*, Aksant 2004).

Dirk Stemerding, Lene Koch & Pascale Bourret, DNA diagnosis and the emergence of cancer genetic services in European health care. *European Journal of Human Genetics, 5 (2),* 1997: 25-30 (also published in a more comprehensive version in: P. Wheale, R. von Schomberg & P. Glasner, *The social management of genetic engineering,* London, Ashgate, 1998: 117 -138).