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ABSTRACT This paper compares the development of genetic testing for breast cancer (BRCA testing) in the USA and the UK. It argues that national political cultures played an important role in how these genetic testing technologies were shaped, and that the shapes of these technologies had important implications for the users of these systems. In order to demonstrate the roles of national social and political elements in the development of new genetic testing technologies, I introduce the concept of a technology's architecture, which is made up of components and the specific ways in which these components are assembled to fulfill particular functions. In the USA, four very different BRCA testing systems initially emerged. However, one biotechnology company, Myriad Genetics, eventually used its legal and economic position to become the sole provider of testing. It offered BRCA testing the way many other laboratory tests were provided in the USA, available to anyone through any physician. The shape of this testing service had important implications for its participants, defining the client as a consumer who could demand access to any of Myriad's laboratory services, but could not choose among testing systems. In the UK, the government-run National Health Service provided testing through regional genetics clinics, using family history information to assess risks and triage care. Clients in the UK were defined as citizens and patients, who had the right to equal access to the testing system but could not demand any specific services.

Keywords breast cancer, comparative health care systems, genetic testing, health policy, UK, USA

Architectures of Genetic Medicine:

Comparing Genetic Testing for Breast Cancer in the USA and the UK

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This paper compares the systems of genetic testing for breast cancer that were built in the USA and in the UK in the mid-1990s. It explores how seemingly uniform biomedical knowledge – the discoveries of genes linked to inherited susceptibility for breast and ovarian cancer (known as the BRCA genes) – was incorporated into medical care in two countries that have very different health care systems but similarly strong commitments to genetics and biotechnology research. One might easily assume that BRCA testing systems in the USA and the UK would be very similar because they focused on the same phenomenon: mutations in the BRCA genes that might lead to increased risk of breast and ovarian cancer.

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Traditional tools used in economics or policy studies to compare national health care systems might point us to differences in funding or regulatory policies that constrain access to care. What this paper demonstrates, however, is that national specificities such as laws, institutions, and traditions have much more wide-ranging effects, both in shaping the new genetic testing technology and defining the roles of the individuals and health care professionals who used it.[1] As we shall see, depending on the country of residence, the individual and her blood took very different technological journeys in the USA and the UK.

Comparative Analysis of Technology

Literature in science and technology studies has shown us how social actors play pivotal roles in shaping the development and details of new technologies (Latour, 1987; Bijker et al., 1989; Casper & Clarke, 1998). Most of these approaches, however, are agency-centered, focusing on the importance of individual actors, actants, or social worlds in influencing the shape of a technology.[2] The Social Construction of Technology (SCOT) approach, for example, encourages analysts to follow how relevant social groups define a technology and encourage its development in a particular direction. The actor-network theory (ANT) looks beyond human agency to argue that technologies are the products of a network of human actors and non-human 'actants' linked together to support their development. The social worlds approach foregrounds power dynamics by exploring how invested parties influence the development of technologies. None of these approaches, unfortunately, provides scholars with much guidance as to what occurs outside these relevant social groups and networks. What causes an actor to orient to a technology in a particular way? Why does the development of a technology proceed in one direction rather than another? How should we understand the roles of more persistent social elements such as social norms, legal frameworks, and institutional traditions in the development of technologies?

In recent years, analysts of technology have tried to incorporate such 'structural' elements in their approach. Wiebe Bijker, a proponent of SCOT, introduced the concept of 'technological frames', which directs attention beyond interactions among actors to 'the goals, the ideas, and the tools needed for action' (Bijker, 1997: 191). Whereas the technological frame can incorporate more diffuse social elements because it is external to the actors involved and the interactions among them, it exists only in relation to the development of a specific technology. Bijker (1997:192) notes, 'A structure is being created by actions and interactions, which in turn will constrain further actions and interactions'. Thus, because the technological frame does not predate the technology or exist independently of it, we cannot trace how persistent elements such as traditions and regulatory frameworks might influence the development of the technology.

Thomas Hughes, the primary developer of the systems approach, has also tried to address these structural issues by introducing the concept of technological 'styles', which include 'entrepreneurial drive and decisions, economic principles, legislative constraints or supports, institutional structures, historical contingencies, and geographic factors, both human and natural' (Hughes, 1983: 462). While this concept allows Hughes to take national specificities and persistent social elements into account, it does not specify how these styles figure in the development of technology. Exactly what difference, for example, do institutional structures and historical contingencies make in the development of technology? Is there a way for us to study this?

Through in-depth interviews, document analysis, and ethnographic observation, I conduct a comparative case study of genetic testing for breast cancer in the USA and the UK to develop a better understanding of how national specificities influence the development of innovation.[3] I argue that as innovators determine how to build their genomic technologies, they choose among a finite set of possibilities that are framed by existing national laws, traditions, and institutional structures for the provision of biomedical services. They make choices among these possibilities based on their own interests, as well as their vision of what might be easiest to develop successfully. Incorporation of these national repertoires, however, does not mean that a technology develops along a clear, predetermined path. As I will describe in more detail later, innovators not only choose among multiple (and sometimes competing) options, but they reinterpret existing options to build technologies in totally new ways.

The Medical Testing System as a Technology

Before we begin to analyze BRCA testing in the USA and the UK, we first need a framework to compare the testing systems. In order to do this, I shall introduce the concept of a technology's *architecture*. The architecture of a technology, much like the architecture of a building, is made up of components (for example, steel beams and concrete) and specific ways in which these components are fitted together to fulfill specific functions. All medical testing systems, for example, must somehow direct individuals to testing, assess their eligibility, inform them about potential risks, benefits, and implications of the test, extract material or information for testing by a technical apparatus, and report the results. Ultimately, based on the results, various medical management strategies may be implemented. These components are fitted together to fulfill the system's technical and clinical functions.

The way that medical testing systems define and carry out functions, however, can vary considerably depending on the specific test and cultural context. In the USA and the UK, for example, individuals might be directed to a test through the advice of a physician or by newspaper articles and direct marketing campaigns. In addition, market-driven or social welfare objectives of the two systems might respectively privilege technological solutions or preventive methods.

Identifying the architectures of medical testing systems facilitates their comparison by highlighting how similar functions might be carried out in different ways. Consider two common medical testing technologies, amniocentesis and home blood pressure testing. Whereas equipment for testing blood pressure can be purchased in a drugstore and used by an individual in the privacy of her bedroom, amniocentesis must be conducted in a clinical setting and requires the participation of a laboratory to analyze the biological material. Highlighting these similarities and differences can also be very important for understanding the role of national context in the development of these technologies; focusing on the components that make up these architectures can help us understand their origins and how and why they were used.

Defining the Users of the Testing System

This paper also demonstrates how the architectures of these testing systems have important implications for their users. Many scholars argue that genetic testing defines individuals whose blood is drawn and analyzed in terms of at-risk classifications based on genetic information, resulting in changed perceptions of self and familial relationships, and obligating specific actions (Hallowell & Richards, 1997; Lock, 1998; Novas & Rose, 2000). But what influence does testing have on the roles of individuals and providers within the health care system itself? Does the individual whose blood is drawn and analyzed (to whom I will refer as the 'client'[4]) resemble a traditional patient, a consumer, a citizen, or something else?

This paper considers how the architecture and components of a testing system and the way they fit together shape the roles of participants in the system – including not only testing clients, but health care professionals and test providers as well. I focus on how the system's architecture articulates the rights, responsibilities, and authority of its users.[5] To explain this focus, let us return to the comparison of the at-home blood pressure testing kit and amniocentesis. When a person interested in testing her blood pressure purchases a test kit, she becomes a consumer with the right to demand the test, and the freedom to choose whether to interpret the test results herself or seek the guidance of a health care professional. In contrast, someone undergoing amniocentesis, which is only available in the clinical setting, seems like an ordinary patient who has restricted access but the guidance of a health care professional. As we can see, these aspects of system participants are also intertwined with one another. In the amniocentesis system, the patient's rights depend upon the physician's responsibilities and authority. The physician makes the ultimate decision about access to amniocentesis. She, in turn, is subject to rules and standards from professional organizations, as well as the hospital in which she practices. These standards define who the physician can test and how they should be tested (professional organizations may advise physicians not to allow amniocentesis for gender selection purposes, whereas hospitals may require that patients provide evidence that they can pay before access to testing is granted). Of course, the architectures of these systems do not unequivocally determine the identities of testing system participants. They do, however, guide and constrain them, and comparing these processes can help us better understand the relationship between genetic technologies and users' identities.

The development of genetic testing for breast cancer in the USA and the UK provides a particularly interesting case study because it was the first genetic testing technology available in both countries for a common disease. It marked a shift in genetic testing technology, from relatively simple tests for Mendelian disorders that could identify mutations that predicted disease with certainty, to susceptibility tests that merely predicted a range of disease risks. Only 5–10% of all breast cancers result from mutations to the BRCA genes, but each of the hundreds of mutations to those genes predicts a different incidence of breast and ovarian cancer (ranging from 30 to 85%; Ford et al., 1994; Easton et al., 1995; Struewing et al., 1997). Thus, not only does this case provide a rich story of the relationship between national context and the development of medical technologies, but it also provides insight into how genomic medicine is incorporated into contemporary societies.

In what follows, I compare the four main BRCA testing services that were initially built in the USA in terms of their architectures and implications for users. I then describe how one of these providers, a biotechnology company, used its intellectual property rights and economic position to become the sole provider of BRCA testing in the USA.[6] I then describe the architecture and implications of the British government-run BRCA testing services. Finally, I conclude with some general remarks on how research on the relationship between national political cultures and technologies can contribute to social studies of technology.

The USA: The University of Pennsylvania's Genetic Diagnostic Laboratory

As a first step in examining the variety of BRCA testing system architectures in the USA, let us consider the University of Pennsylvania's Genetic Diagnostic Laboratory (GDL). GDL, which set up its testing service in 1995, offered BRCA testing only in the context of its own research, and required clients to undergo counseling at an academic medical center.

As a research laboratory at the University of Pennsylvania, one of the country's leading academic medical centers, GDL operated according to the dual priorities of research and health care common among academic medical centers in the USA.[7] These dual priorities guided the architecture of GDL's services, and specifically, its BRCA testing system. Since the early 1990s, the laboratory had been developing a cheaper and faster alternative to DNA sequencing called conformation sensitive gel electrophoresis (CSGE; Ganguly et al., 1993; Williams et al., 1995). GDL had refined this technique by offering testing services to the public for a

number of rare diseases and in 1994 they decided to develop a testing service for BRCA genes that would provide them with the opportunity to demonstrate the utility of CSGE even further: they could show that their technique could find mutations in long and complicated susceptibility genes.[8]

As they built and provided their services, GDL and all other genetic test providers were subject to only minimal regulation by the US government. While patient activists, bioethicists, scientific and medical organizations, and government advisory committees had for years encouraged the Food and Drug Administration (FDA) to regulate clinical and technical dimensions of genetic testing (areas over which the FDA had jurisdiction), they had been unsuccessful (National Breast Cancer Coalition, 1996; Task Force on Genetic Testing, 1997).[9] In fact, the FDA only regulated the 'analytic validity' of genetic testing services, assessing laboratory facilities in order to ensure that laboratories were able to conduct proper molecular analyses using appropriate reagents and equipment.[10]

A Client's Journey Through the Genetic Diagnostic Laboratory Testing System

Despite the lack of government regulations, GDL incorporated concerns of the patient advocacy genetics communities that BRCA testing was not yet ready for widespread use and built its BRCA testing system quite differently than its other laboratory services. Whereas clients interested in other tests offered by GDL could have their blood drawn and sent to the laboratory by any physician, GDL required that clients interested in BRCA testing first visit a genetics clinic at an academic medical center. GDL did not advertise its BRCA testing service directly to the public. Instead, potential clients learned about GDL's system either through their own initiative in contacting an academic medical center directly or through a physician's referral. This gatekeeping mechanism was intended to ensure that clients received counseling from a health care professional specially qualified in genetics, who would explain genetic risk and the benefits and risks of testing.[11]

Except for requiring clients to access its testing service through a genetics clinic at an academic medical center, GDL did not involve itself further in the clinical interaction. In delegating responsibility over test users to the genetics clinic, GDL probably assumed that a genetics specialist would gather family history information to assess the likelihood that the client had a genetic mutation and make a recommendation about whether testing would be beneficial for her. This family history information would also be helpful after testing had been conducted, as it provided clients with additional information about how a mutation might affect their risk of future disease. Depending on the client's family history and lifestyle information, health care professionals at the genetics clinic would offer some the opportunity to participate in a research study that would cover payment for laboratory analysis. These studies usually investigated the psychological impact of testing or the utility of testing for disease prevention and/or management. This approach to BRCA testing was consistent with prevailing views in the medical genetics community, as well as with the recommendations of scientific and medical organizations and patient activist groups. They felt that uncertainty over the relationship between specific BRCA gene mutations and disease incidence as well as the psychological implications of being identified as at-risk justified the need for extensive counseling in the context of laboratory analysis (American Society of Human Genetics, 1994; American Medical Association, 1996; American Society of Clinical Oncology, 1996; National Action Plan on Breast Cancer, 1996; National Breast Cancer Coalition, 1996; Task Force on Genetic Testing, 1997).

If the client decided to undergo BRCA testing, she (through her health care professional) sent a blood sample to GDL's laboratory. In addition to the sample, GDL required that the health care professional and patient send payment (US$700 for testing the BRCA1 gene and US$1500 for testing both BRCA genes) as well as completed forms that documented medical and family history and written proof of consent to the testing procedure.[12] Once GDL received the blood sample and other materials, researchers tested it using CSGE, the experimental DNA analysis technique they were trying to refine. The family history information included with the blood sample helped GDL researchers to determine where to look for a BRCA gene mutation (certain patterns of family history suggested specific mutations, or even mutations in a particular gene).

The test result that GDL returned to the health care professional and client at the academic medical center indicated whether or not a mutation had been found and, if a mutation had been found, what likelihood of risk it conferred. It was up to the staff at the genetics clinic to help the client understand the test result. GDL was no longer involved. If the test result showed the client positive for a BRCA mutation, staff at the genetics clinic informed her about the meaning of such a mutation and instructed her about options for managing BRCA risk. The responsibility of clinical management was then left up the client, who decided how to proceed with her clinical care. In fact, unless the client specifically requested the communication, neither GDL nor staff at the genetics clinic conveyed the results of the BRCA test to the client's primary care physician. This standard practice at genetics clinics in the USA responded to concerns that genomic information on the medical record could fall into the hands of insurers or employers and cause discrimination. This reluctance to include genomic information in the medical record, however, could impede continuity of care when primary care physicians lacked information about potentially significant genetic test results.

Defining the Roles of Participants

As the earlier discussion suggests, the architecture of GDL's BRCA testing service shaped the roles, rights, responsibilities, and authority of participants in its testing system. Whereas GDL adopted an approach that was familiar to many academic medical centers in the USA by providing

laboratory services to help finance its research goals, it did play a greater role than its counterparts in defining who could participate in its BRCA testing system. Only specialist health care professionals trained in genetics and employed at academic medical centers could provide clinical care to clients, and clients were likely to be subjected to stricter eligibility criteria because they could only access GDL's system through a specialized clinic. Eligibility was usually determined on the basis of a client's personal or family history of breast and ovarian cancer. In addition, access tended to be limited to those who lived or worked within a short distance of a center and were aware of the specialized services it offered. While GDL only allowed health care professionals affiliated with a genetics clinic at an academic medical center to provide testing services, it did not attempt to manage the interaction between the health care professional and client. The health care professional was the ultimate authority for determining whether to recommend testing, to allow participation in research protocols, or to prescribe counseling before and after testing.

The USA: OncorMed

OncorMed, a medium-sized start-up biotechnology company based in Gaithersburg, MD, USA, also offered BRCA testing in a research context. The architecture of its testing service, however, differed considerably from that of GDL. It incorporated the priorities of a start-up biotechnology company while paying attention to the concerns of many in the US medical genetics community who felt that BRCA testing should only be offered through clinical research protocols. Rather than providing testing in order to refine an experimental laboratory technique, OncorMed's protocols were designed to ensure strict attention to counseling and limit access only to high-risk individuals.

OncorMed, a subsidiary of molecular biology products company Oncor, Inc., was created in July 1993 as a company focused on using genetic discoveries and technologies to improve medical care for cancer. Unlike some biotechnology companies that simply looked for disease genes and developed diagnostics and therapeutics based on these discoveries, OncorMed not only searched for genes linked to inherited susceptibility for cancer and built genetic testing technologies, but also developed medical management tools to help physicians identify individuals who had increased risk for cancer and might benefit from the company's technologies.[13] This involvement of a start-up biotechnology company in cancer genetics research and development, particularly at such early stages of innovation, was a uniquely US phenomenon. Over a number of decades, the US had developed a network of laws that encouraged start-up companies to accelerate commercialization of research through both venture capitalist funding and relationships with government-funded academic researchers (Kenney, 1998).

In keeping with this overall strategy to integrate state-of-the-art technology with medical practice, OncorMed sought to develop a BRCA testing service and conducted research to find the BRCA genes. In 1994, it applied for a patent covering a sequence of the BRCA1 gene that would provide it with proprietary rights covering any downstream invention, including testing services.[14] The company was not, however, the only entity applying for patents covering the BRCA genes and in order to strengthen its proprietary position even further, it amassed licenses covering the BRCA1 (and eventually the BRCA2) genes. It purchased a license on Mary-Claire King's BRCA1 patent, which covered a number of markers on the BRCA1 gene, and also negotiated a license on the BRCA2 gene patent held by Mike Stratton at the Institute for Cancer Research in London.

When negotiating a license agreement with Stratton, OncorMed agreed to stipulations that would limit its monopoly power and influence the way the patent would be employed in clinical practice.[15] Among its many requirements, the agreement specified not only that clients be counseled before and after testing, it also provided a list of topics that counselors had to cover.

Stratton's counseling guidelines and desire to couple counseling with laboratory testing fitted in well with OncorMed's interest in incorporating new genomic technologies into medical care.[16] This dedication to influencing clinical services, not stand-alone testing as conducted in the laboratory medicine tradition, was also reflected in the company's choice of Patricia Murphy, a medical geneticist who was board-certified in both clinical cytogenetics and molecular genetics, to build and direct its BRCA testing service. Murphy had served as a member of two federal advisory committees, the National Institutes of Health (NIH)'s Task Force on Genetic Testing and the US Department of Health and Human Services National Action Plan on Breast Cancer (NAPBC) Hereditary Susceptibility Working Group. Both had recommended that much more research needed to be conducted with regard to the clinical, psychological, and social implications of genetic testing, and that overall, the new technology should only be provided in the context of counseling.

Murphy sought to develop a service that would integrate counseling and testing and be acceptable to the medical genetics community. She voluntarily decided to follow the stringent recommendations of the NIH Task Force and Hereditary Susceptibility Working Group, as well as the American Society of Human Genetics and the American College of Obstetrics and Gynecology. OncorMed would offer BRCA testing only in the context of clinical research.

Research was not required by the terms of Stratton's license and recommendations of these advisory groups did not carry the force of law. In principle, Murphy could have simply offered OncorMed's BRCA testing service to anyone who wanted it, relying on Stratton's counseling guidelines and OncorMed's previous training efforts to assure that patients received appropriate counseling. The company's role could have been limited to analyzing blood samples and returning results about the client's mutation status to the health care professional and client. It also could

have developed an approach similar to GDL's, ensuring appropriate attention to clinical care by restricting access to clients who accessed medical centers.

However, OncorMed's restriction of testing to the research context not only demonstrated concern about the psychosocial dimensions of testing and a willingness to work with the norms and priorities of the medical genetics community, but it also certified this commitment because all clinical research protocols at academic medical centers had to be approved by an Institutional Review Board (IRB). According to US law, all research protocols conducted by investigators at an institution that receives a federal grant must be approved by an IRB, an ethics board usually made up of physicians, scientists, bioethicists, and representatives of the public.[17] An IRB examines all research protocols conducted at an institution in order to ensure that they are ethically sound and scientifically valid.

Of course, OncorMed was also a private company that needed to turn a profit in order to please its partners and stockholders. How could it reconcile its commitment to limiting testing services to high-risk women with its need to generate revenue and produce profits? OncorMed decided to create its own IRB-approved research protocols, to expand the distribution of its BRCA testing service while maintaining its commitment to medical care.[18] This is particularly interesting, because as a private company receiving no federal funds, OncorMed was under no legal obligation to convene an IRB to approve its research protocols. But, such a move would allow the company to maintain a balance between its commercial objectives and commitment to excellent care. It could increase its potential market by including individuals who did not have easy access to an academic medical center, while also empowering a governing body which could certify that the company operated in the best interests of the users of its testing system. Unlike GDL's system, where IRB approval was only a factor for a fraction of its clients, IRBs (albeit multiple ones) would regulate all users of OncorMed's testing system. The regulations covered interactions between principal investigators and clients being tested at academic medical centers, as well as engagements between OncorMed, health care professionals, and research subjects involved in the company's research protocols.

A Client's Journey Through OncorMed's Testing System

In order to access OncorMed's testing system, a client needed to be defined as high-risk and access a research protocol either at a specialized genetics clinic or through OncorMed's main facility. Definitions of high-risk, however, were not standardized and often varied depending on the protocol.

After a health care professional helped a client enroll in a research protocol, she counseled her. Unlike GDL, which left the details of the counseling interaction up to the health care professional, OncorMed exerted control over the counseling process. The company not only provided health care professionals with the Stratton guidelines, but also collected affidavits from them certifying that they had covered these topics, which included the benefits and risks of testing for the client and her family, in the counseling session.[19] If the client consented to laboratory analysis after the counseling session, her blood was drawn and sent to OncorMed, along with payment, medical and family history information, the counseling affidavit, and documentation of informed consent.

When OncorMed received these materials, it began a laboratory analysis that differed significantly from GDL's process. While GDL was experimenting with a new method of DNA analysis and examining the full sequences of both BRCA genes, OncorMed used a step-by-step approach to find a gene mutation in high-risk families. First, the laboratory searched for BRCA gene mutations that were well known and frequently occurring. If the laboratory's search found no mutations, it then conducted protein truncation testing (PTT),[20] which was said to be 80% sensitive, for unknown mutations in regions of the gene where mutations were likely. If the laboratory still found no mutations, it sequenced the rest of the gene. Payment for the laboratory analysis followed this step-by-step approach. The initial search for mutations cost US$500, PTT cost US$800, and the final sequencing cost US$800.

After testing, OncorMed returned the results to the health care professional. Its involvement ended there. The health care professional then reported the results to the client and described future options for management. However, the client using OncorMed's system, like her counterpart in GDL's system, made the ultimate decision about how to incorporate the test results into her medical management.

Defining the Roles of Participants

At this point, we can see differences between the roles of the participants in GDL's and OncorMed's systems. OncorMed took interest in both the technical and clinical dimensions of testing, and exerted much more explicit control than GDL over both the health care professional and client. While GDL restricted the types of participants in its system by requiring clients to pass through an academic medical center, OncorMed shaped both the identities of the participants as well as the interaction between them by providing counseling guidelines and restricting access to high-risk individuals enrolled in research protocols.

The client's role as a research subject was quite different in OncorMed's system than in GDL's. While GDL's laboratory research did not affect the subject's clinical experience (and only a subset of GDL's subjects were enrolled in clinical research protocols), OncorMed's subject had to be defined as high-risk according to the academic medical center or the company, and had a standardized counseling experience. She could, however, access OncorMed's system through any health care professional, not just those at academic medical centers.

The health care professional in OncorMed's testing system had to accept restrictions on her authority. She had to be willing to work with OncorMed's research protocols or engage in research of her own. She had to abide by the company's eligibility criteria and promise to cover certain topics in her counseling session. Furthermore, these counseling requirements not only shaped the health care professional's clinical activities, but also defined the substance of the interaction between the health care professional and client.

The USA: The Genetics and In Vitro Fertilization Institute

The Genetics and In Vitro Fertilization Institute (GIVF), a private reproductive and genetics services clinic, offered BRCA testing using a different approach than GDL or OncorMed. It offered BRCA testing as an integrated service of genetic counseling and laboratory analysis for a single fee under one roof.[21] GIVF's service, however, was not useful to everyone, as its method of laboratory analysis searched only for the BRCA gene mutations common among individuals of Ashkenazi Jewish descent. As such, its choice of laboratory analysis served as an inadvertent gatekeeping mechanism that restricted access differently than had GDL's or OncorMed's.

GIVF was founded in 1984 by Joseph Schulman, a pediatrician and obstetrician, who was the only student of Robert G. Edwards and Patrick Steptoe, the UK inventors of in vitro fertilization. It originally focused on providing prenatal genetic testing and other reproductive services, such as in vitro fertilization and egg and sperm donation and retrieval. By the 1990s, however, it had also developed a large menu of tests, including those for biochemical markers (for example, α-fetoprotein), chromosome abnormalities (for example, amniocentesis), and DNA mutations (for example, Fragile X syndrome, Canavan's disease, Tay-Sachs, and sickle cell anemia). GIVF was the first provider of genetics and infertility services to offer both medical care and laboratory testing under one roof: with services including initial appointment, counseling about the procedure, laboratory analysis, and follow-up visits.

With more than 300 employees, GIVF described itself as 'the country's largest private clinic offering reproductive and genetics services'.[22] It certainly had the resources to add another genetic test to its already large menu, and it was also a very highly visible and well-established provider with a large clientele. Company officials were also particularly keen to offer testing because inherited susceptibility had touched the personal life of its Chief Exective Officer, Joseph Schulman. His wife, and her mother, grandmother, and great-grandmother, all of Ashkenazi Jewish descent, had had breast cancer. His wife had wanted to be tested, but could find no tests available outside the context of a research protocol (Kolata, 1996). In light of Schulman's wife's situation, and given GIVF's size and resources, it is not surprising that in April 1996 GIVF became the first provider to launch a commercial BRCA testing service. Because it only tested for the three BRCA gene mutations common among the Ashkenazi Jewish population, it was a very simple test to develop. The institute first offered the test to women affiliated with GIVF and their families, but soon expanded the service and began marketing it more widely.

The launch of the first commercial BRCA testing service, however, stimulated tremendous controversy from a number of scientists, activists, and bioethicists, who felt that GIVF had violated an informal agreement in the genetics community not to provide testing commercially until more research had been conducted. These critics published their opinions in newspapers and scientific journals, arguing that it was premature to offer testing outside the context of research, particularly when numerous questions remained about the risks posed by gene mutations and the effectiveness of medical management options (Brenner, 1996; Burke et al., 1996; Hubbard & Lewontin, 1996; Koenig, 1996). They were also concerned that GIVF marketed its testing service directly to the public, through advertisements in Jewish newspapers and in the *New York Times*.[23]

Like the other testing providers, however, including those who offered BRCA testing in the context of research, GIVF was under no legal obligation to heed these critics. In fact, company officials argued instead that BRCA testing was a life-saving technology that would 'be a powerful force in the struggle to reduce the tremendous morbidity and mortality of cancer' (Schulman & Stern, 1996: 244). GIVF further justified its testing service by noting that it was only providing testing for BRCA gene mutations that had a well-demonstrated relationship with breast cancer. GIVF's justification of its testing service highlights an important tension in the development of contemporary genetic medicine. Whereas genetics research and the development of genetic diagnostics and therapeutics targeting close-knit ethnic groups such as the Ashkenazim could possibly result in medical interventions for members of that population, many critics also argue that the development of such targeted testing, particularly in the absence of effective therapeutics, may lead to widespread discrimination (Duster, 1990; Nelkin & Tancredi, 1994; Rothstein, 1997).

A Client's Journey Through The Genetics and In Vitro Fertilization Institute's Testing System

In order to access GIVF's integrated service of counseling and laboratory analysis, clients had to visit one of its clinics in Virginia or Maryland. Once a client arrived at GIVF's offices, she met with a staff geneticist or genetics counselor, who gathered information about family history and discussed with her the meaning of the BRCA genes, GIVF's testing system, the benefits and risks of testing, and the possible implications of testing positive for a BRCA gene mutation. If the client wanted to pursue testing she would pay (US$295 for the integrated testing and counseling service), give written certification of informed consent, and have her blood sample taken. Unlike OncorMed, which allowed only individuals with extensive family histories of breast and/or ovarian cancer access to its system, GIVF

was adamant that family history was an inaccurate predictor of the BRCA gene mutations common in the Ashkenazi Jewish population (Schulman & Stern, 1996: 247). Thus, GIVF never rejected anyone, even if they had no family history of breast or ovarian cancer or were not of Ashkenazi Jewish descent. It is safe to assume, however, that most users of GIVF's testing system were self-selected members of the Ashkenazi Jewish population.

The blood sample was then sent to GIVF's in-house laboratory, which screened it for the three mutations common among the Ashkenazim. Because GIVF only checked for three mutations, its methods of DNA analysis were much simpler and cheaper than GDL's or OncorMed's. Once laboratory analysis was complete, the GIVF staff member met again with the client and conveyed the test results. If the results were positive, the staff member and individual typically discussed possible options for clinical management. As with OncorMed and GDL, GIVF's involvement in the client's health care stopped at that point. GIVF did not send test results back to the primary care physician unless the client requested them, nor did it involve itself in the client's post-test clinical management.

Defining the Roles of Participants

Unlike GDL, which restricted access to testing to academic medical centers, and OncorMed, which used counseling guidelines, eligibility criteria based on familial risk, and research protocols to frame the roles of both health care professionals and clients, GIVF managed participants by building a system under one roof. It employed the health care professionals who delivered the tests and, by providing them with both formal and informal training, also guided their counseling practices. Health care professionals affiliated with other institutions or clinics played virtually no role in the system, except perhaps through referral and for helping to direct the client's care after the test results had been returned.

Whereas the client who wanted to use GIVF's testing system might be considered a consumer because she could buy testing for a US$295 fee and her access was not explicitly restricted in any way, her freedoms were shaped by the architecture of the testing system in many ways. First, she could only access GIVF's offices in Virginia or Maryland, suburban areas easily accessible only by automobile. Second, the client who used GIVF's testing system was required to undergo counseling. She could not choose to skip the counseling process and simply use the laboratory testing service. Third, she could only have access to tests for the three mutations common among the Ashkenazi Jewish population. GIVF's method of laboratory analysis thus influenced the types of clients who used its testing system.

GIVF's focus on the Ashkenazi Jewish population rested on earlier medical (and specifically genetic) interventions based on race and ethnicity. A number of screening programs in the USA, such as those for Tay-Sachs and sickle cell anemia, targeted particular ethnic groups because of evidence of higher mutation incidence in those populations. By the late 1990s, a number of providers offered panel tests that screened for mutations in a variety of diseases common among the Ashkenazim.[24] Many laboratories offered tests for this population because its small size and high intermarriage rate often led to a small and discrete set of mutations that could be easily analyzed.[25] By providing a commercial testing and counseling service for the three mutations common in the Ashkenazi Jewish population, GIVF provided members of this population with an easy opportunity to understand their genetic risk for breast cancer.

The USA: Myriad Genetics, Inc.

My fourth example is Myriad Genetics, a start-up company based in Salt Lake City, Utah. Myriad, like GIVF, offered BRCA testing as a commercial service, but shaped its testing system differently. Rather than offering a package of genetic counseling and laboratory analysis, Myriad treated BRCA testing as an ordinary medical test: the physician ordered the test, sent payment and a blood sample to the laboratory, and the laboratory furnished the results. As a private company, however, Myriad also marketed its system widely to physicians and the public. In effect, Myriad treated BRCA testing as a state-of-the-art product that should be available on demand to all women.

In 1991, scientists at the University of Utah formed Myriad Genetics Inc. in order to capitalize for gene discovery efforts on the genealogical data that had been collected from large Mormon families over centuries. It began looking for one of the most highly sought after genes, BRCA1, soon after Mary-Claire King localized it to chromosome 17 in 1991. Searching for such a highly anticipated gene attracted investment in the company, and by 1992 it had entered into a 3-year collaboration with Eli Lilly, a multinational pharmaceutical company. Under the terms of the agreement, Lilly provided the company with US$1.8 million in return for an exclusive license for any diagnostic kits or therapeutic products resulting from a breast cancer gene discovery (Myriad Genetics, Inc., 1995). In 1994, Myriad announced it had mapped and sequenced the BRCA1 gene, and by 1995, the company announced that it had mapped and sequenced the BRCA2 gene as well.

Soon after these announcements, Myriad set about developing a service that would test for mutations in both genes. Like many of the other start-up biotechnology companies formed in the USA during the 1980s and 90s, it applied for patents on its discoveries. After applying for patents on both genes, the company could have chosen simply to profit by licensing them to other companies. Instead, Myriad decided to build its own BRCA testing service. While the reasons for this decision are perhaps only fully understood by Myriad executives, an outside observer can surmise that the company hoped to achieve several goals: to reap immediate revenue from the testing service; to develop a database on BRCA genes tested (and mutations found) that might eventually yield insight for therapeutic developments; and to sell or license the database to other

companies. Because markets for genetic diagnostics were considerably smaller than for therapeutics, it is quite likely that a genomic database would generate considerably more revenue than a BRCA testing service.

Myriad framed itself as a private diagnostics laboratory, an organizational form that was quite familiar in the US context, and built a BRCA testing system that was consistent with its goals. Physicians would send a client's blood sample, along with payment, to the laboratory, and the laboratory would conduct DNA analysis and return the result. It defined many medical issues as being outside its scope, such as how clients would be counseled about testing and how results would be conveyed. A company official noted, for example, how difficult it would be to assure the quality of genetic counseling:

> You know, are we going to have to have people pass some sort of exam, how are we going to ensure the quality of genetic counseling. . . . And I can tell you, there were many many discussions about, let's just hire a bunch of genetic counselors and provide genetic counseling. Sort of the way, sort of the way that Genzyme [another genomics company] does it. And we did think about that very closely as well, and didn't feel that that was meeting the goals of where we wanted to go in the laboratory.[26]

Myriad also allowed clients to access its testing system through any physician, in contrast to GDL who required clients to access its testing system through academic medical centers, OncorMed who restricted testing to clients enrolled in research protocols, and GIVF who limited BRCA testing clients to its clinic. Myriad's client could choose to visit a genetics clinic or ask her family physician to help her gain access to BRCA testing. This diversity of health care professionals available to clients meant that counseling could vary considerably. If a client visited a specialist at a genetics clinic, for example, she would expect to receive the benefits of training, specialization, and experience in genetics counseling. Critics have argued that primary care physicians are less likely to have formal training in genetics or genetic counseling, or to have the benefit of a network of colleagues (both at the institution and in professional associations) with relevant knowledge and experience (American Society of Human Genetics, 2000).

Myriad also did not place any explicit restrictions on who could access its testing system. Unlike OncorMed, which only tested clients deemed to be high-risk, Myriad did not even require health care professionals to record a full family history of breast and/or ovarian cancer. Physicians were free to refer whomever they chose for testing. Myriad required only that the health care professional send it the blood sample, along with payment and informed consent.

A Client's Journey Through Myriad's Testing System

Whereas it defined itself as a laboratory that simply provided a DNA analysis service, Myriad still marketed its product widely to physicians and directly to women. It advertised its service in a variety of publications, including playbills on Broadway, airline in-flight magazines, and the *New York Times* magazine.[27] By 2002, the company had expanded its campaign to include advertisements on radio and television, as well as in major women's magazines such as *Better Homes and Gardens* and *Good Housekeeping*.[28] All of these advertisements provided clients with the company's toll-free number and website address for more information about its BRCA testing services.[29] By combining the model of an independent diagnostic laboratory with mass-marketing, Myriad sought to increase its revenue from testing and, through increased testing, expand its database. Not only might physicians suggest BRCA testing to their patients, as they often did with other sorts of laboratory tests, but patients might themselves initiate an inquiry.

Myriad offered four types of laboratory analysis: analysis of the three mutations common among the Ashkenazi Jewish population (about US$450); full sequence analysis of both BRCA1 and BRCA2 genes (about US$3000); Rapid BRACAnalysis™, which provided full sequencing of the BRCA1 and BRCA2 genes with results returned to the physician within 2 weeks (about US$4000); and single mutation analysis (about US$250), usually done after a mutation had been found in a family.[30] Myriad's methods for analyzing the BRCA genes differed considerably from those conducted by GDL and OncorMed. While all of these providers checked both BRCA genes for mutations, Myriad generated information about the full sequences of the BRCA genes and then checked for mutations while GDL targeted mutations and OncorMed both targeted mutations and sequenced parts of the genes. Myriad's laboratory methods reflected its priorities. Generating sequence data about the BRCA genes would be useful for the company's database, and its focus on providing a 'sophisticated' laboratory analysis would reinforce the company's self-definition as merely a diagnostic laboratory.

After Myriad tested the blood sample, it sent the test results, which identified the mutation and the range of increased risk for future disease, back to the requesting health care professional. As with GDL and OncorMed, Myriad no longer played an active role in the testing system once it returned test results.

Defining the Roles of the Participants

By defining itself as a commercial diagnostic laboratory that simply offered a DNA analysis service, Myriad drew clear functional and temporal boundaries around the aspects of the testing system that were under its purview. Unlike the other testing providers in the USA, it did not attempt directly to control how clients gained access to its system or how they were counseled. It also did not try to manage how health care professionals conveyed test results to clients. It restricted its focus to providing a DNA analysis service after a client's blood reached its laboratory. Thus, while it marketed its test directly to physicians and their clients, it did not try to manage their interaction.

This approach meant that Myriad did not directly interfere with the authority of the health care professional. Decisions about client eligibility and counseling methods before and after testing were left up to the health care professional's discretion. In addition, Myriad did not restrict use of its system to particular health care professionals, but instead gave access to any physician. By allowing the client to choose any physician, however, Myriad unintentionally restricted the authority of the health care professional. Rather than being subject to the clinical judgment of a particular specialist or the eligibility criteria of a research protocol or genetics clinic, clients could seek out the help of any physician who would facilitate their access.

While clients in GIVF's and Myriad's systems may both be considered consumers, because they received BRCA testing services in exchange for direct payment to the test provider, each was defined quite differently. While GIVF's consumer was able to demand access to testing, she had to use a standardized counseling and laboratory analysis. Myriad's consumer was free to choose both the type of clinical care (counseling at a genetics clinic or no specialized care at all) and the type of laboratory analysis. Myriad characterized this unfettered consumer choice as empowering, arguing that by choosing to purchase genetic information, clients could make their own health care decisions. Many breast cancer activists, however, disputed Myriad's claim, arguing that the provision of genetic information, particularly in the absence of clear information about the degree of risk conferred by a gene mutation and 100% effective preventive measures, was actually dangerous and disempowering (Breast Cancer Action, 1996; National Breast Cancer Coalition, 1996). As I have argued elsewhere, while the old cry of women's health movements, 'Knowledge is power', seems so simple and straightforward, the relationships between genetic information, consumer choice, and empowerment are complicated indeed (Parthasarathy, 2003).

Emergence of a Single Testing System

By 1997, GDL, OncorMed, GIVF, and Myriad had built four very different systems to provide genetic testing for breast cancer in the USA. However, this environment – in which multiple systems existed and, to some extent, competed with one another – did not last long. Myriad Genetics, backed by its strong intellectual property position, embarked on a campaign to drive its competitors out of the BRCA testing business. Using a combination of threats and bargaining, it forced the other testing providers out of the market by 1999.

As mentioned earlier, immediately after the gene discoveries in the mid-1990s, both Myriad and OncorMed applied for a number of patents and licenses on various aspects of the sequences, mutations, and methods of testing for the BRCA1 and BRCA2 genes.[31] Patents such as these serve as an important currency in the biotechnology industry. They have great value for inspiring investment by suggesting that a company is vigorously pursuing innovation, and after a company's cash flow ends, they are often the major items of value left that might encourage purchase by a large multinational corporation. By 1997, the US Patent and Trademark Office (USPTO) had granted OncorMed and Myriad five patents covering various aspects of the BRCA1 gene sequence.[32] Because both companies offered testing that analyzed the BRCA genes, however, they interfered with each other's patents. Both decided to resolve the situation through litigation, and filed a total of three lawsuits against each other.

After lawsuits had continued for almost a year, OncorMed decided that maintaining its BRCA testing service was not enough of a priority to justify continuing litigation against Myriad.[33] The lawsuits were settled out of court, and in May 1998 Myriad bought OncorMed's patents and testing services for an undisclosed sum. Myriad had used legal and economic means to eliminate OncorMed's testing service, and as a result, the company's investigational testing regime.

This resolution was clearly important for Myriad's overall strategy. First, eliminating competitors would likely result in a much larger market for its test, and therefore a bigger revenue stream. Second, strengthening its intellectual property portfolio could be extremely valuable for attracting funds from venture capitalists and private investors. Finally, by controlling all of the BRCA testing conducted in the USA, the company could develop a comprehensive database that contained details of the BRCA genes (for example, mutation frequency in the US population).

Armed with its own patents and those it acquired from OncorMed, Myriad then sought to shut down the services of both GIVF and GDL.[34] In early 1998, Myriad sent both of them letters to 'cease and desist', arguing that their services violated its BRCA patents by providing testing in return for payment.[35] While GIVF acquiesced quickly, GDL resisted, arguing that it was only providing testing in research protocols that were exempt from Myriad's proprietary reach. Myriad disagreed, insisting that by giving results to, and receiving payments from, health care professionals, GDL was providing a commercial service that violated its patents. This conflict, over what constitutes research and what is defined simply as health care, highlights an ambiguity that is frequently controversial in US biomedicine (Löwy, 1997). This problem arises in many contexts. For example, principal investigators of clinical research protocols provide health care to patients as they study the safety or efficacy of a drug or medical practice. By the same token, physicians providing clinical care outside the context of research protocols often publish details of interesting clinical cases in leading medical journals. IRBs often deal with the difficulties of distinguishing between 'research', which is under their purview, and 'clinical care', which is not. This problematic boundary was contested in the negotiations between Myriad and GDL.

In order to strengthen its position that its service was restricted to research rather than clinical care, GDL began to limit its testing service to clients who were enrolled in research protocols within the National Cancer Institute's (NCI) Cancer Genetics Network, a group of researchers funded

by the NIH. Myriad, unimpressed by this move, sent GDL another letter contending that so long as GDL disclosed results to the patient, GDL was providing a commercial service and violating the patent.[36]

After a series of negotiations, Myriad forced GDL to shut down its BRCA testing laboratory. GDL could only conduct its own research protocols that did not involve any disclosure of results to the client. This resolution, which arose through a combination of Myriad's patent rights and legal resources and GDL's reluctance to engage in a prolonged legal battle with the company, allowed Myriad to control the definition of research and impose its definition of the boundary between research and commercial service.

By setting itself up as the sole provider of BRCA testing in the USA, Myriad further shaped the rights of both health care professionals and clients. Although a client could still choose the health care professional who would facilitate her access to testing and analysis, she now could 'choose' from only one testing system – Myriad's. Similarly, health care professionals, who previously had the freedom to decide which of the different BRCA testing systems suited their needs and clinical philosophy, were now forced to use Myriad's services for their clients.

The UK: Regional Testing Systems

When the BRCA genes were discovered in the mid-1990s, regional genetics clinics run by the UK National Health Service (NHS) also began to develop services to test for BRCA mutations. The clinics modeled their systems on other genetic testing services they provided – as a package of counseling and laboratory analysis connected to specialist and primary care physicians through a hierarchical referral network. While the package of services was somewhat similar to GIVF's system in the USA, BRCA testing in the UK was government-sponsored and oriented towards preventive care.

Since the 1960s the NHS had offered a variety of clinical genetics and genetic testing services at more than 20 regional genetics clinics across the country (Coventry & Pickstone, 1999). These clinics, which were controlled at the regional level rather than by the central NHS administration, provided counseling and laboratory analysis, primarily for Mendelian disorders such as cystic fibrosis. NHS regional health authorities would determine which genetics services were available, and how many tests each clinic could perform per year. UK regional genetics clinics, like GDL and OncorMed in the USA, did not market their testing services to the public. Clients learned about genetic testing services either through their own initiative, or the recommendation of a primary care physician, or a specialist such as an oncologist or surgeon. Clients would visit these clinics at their own initiative or through the referral of a physician, with services paid for by the NHS regional health authority.[37]

Regional genetics clinics developed approaches to BRCA testing services according to their existing infrastructures and the availability of

funds, leading to regional variation in a client's access to these services.[38] Some clinics offered BRCA testing to any client who requested the service until its annual funding allotment ran out. Others restricted testing only to those with a particularly extensive family history of breast and/or ovarian cancer (for example, four or more family members who contracted breast or ovarian cancer before the age of 40 years).

A Client's Journey Through Regional Testing Systems

Once a client came to the regional genetics clinic either on her own initiative or the referral of a physician, she received information and counseling about BRCA testing from a specialist in genetics.[39] This process was similar across clinics, as health care professionals at genetics clinics used informal mechanisms such as conferences and meetings to standardize their practices. During this counseling session, the health care professional informed the client about the risks and benefits associated with BRCA testing and recorded her family's history of breast and/or ovarian cancer. If the client decided to request laboratory analysis, she would return to the clinic for an additional counseling session, during which her blood would be drawn and sent to a regional laboratory for analysis. This counseling process was quite different from Myriad's, as standardized clinical care at the regional genetics clinic became a gatekeeping mechanism for access to laboratory analysis.

Although regional genetics clinics offered BRCA testing services in a standard package of counseling and laboratory analysis, assessments of eligibility for testing and methods of laboratory analysis differed among regions. Regional laboratories used a variety of methods to analyze the BRCA genes. Regions which housed researchers who had conducted studies of the genetics of breast cancer typically offered analysis of the BRCA genes with techniques already used by the laboratory, while other clinics who had not already developed methods for testing those genes often determined laboratory protocols according to the level of funding that they received from the NHS.[40] Some laboratories used CSGE, the technique used by University of Pennsylvania's short-lived testing service, while others adopted PTT, which had also been used by OncorMed (Buckley et al., 1999). Other laboratories simply sequenced regions of the genes in which the most common mutations generally were found.

None of the regional genetics clinics, however, offered a comprehensive, full-sequence analysis of the BRCA genes, like Myriad's in the USA. With its commitment to public health and equal access to care, the NHS's priorities differed considerably from the US company's. Each regional clinic received a fixed amount of funds from the NHS and preferred to spend its allocation on offering tests to as many people as possible, rather than on providing an expensive full sequence test to only a few people. In its 1996 best practice guidelines for dealing with familial breast cancer, for example, the Clinical Molecular Genetics Society (CMGS), the major organization of molecular geneticists in the UK,

focused on the diagnostic and preventative dimensions of testing. Instead of restricting its comments to laboratory practices or promoting a particular method of analyzing the BRCA genes, it emphasized the importance of clinical care in conjunction with testing. The guidelines noted:

> Laboratories are asked to answer two types of clinical questions: diagnostic – is this familial breast cancer? and predictive – is this patient at risk of developing breast cancer? Because breast cancer is so common (lifetime risk of 1 in 8), and because the tests involved are so laborious and expensive, a strong family history must exist before diagnostic testing is undertaken. Criteria should be set (at the clinical level) for deciding which women are to be tested.[41]

While Myriad used its status as a diagnostic laboratory to distance itself from clinical care, laboratory scientists in the UK saw the activities of the clinic as an important part of their remit. In the UK, where genetic testing services were provided by the NHS, even laboratory professionals were concerned with how their activities would influence patient care.

After completing a test, the health care professional met again with the client to discuss the results. In contrast to the US testing systems, many of the UK clinics also shared the results with primary care physicians or other referring physicians in order to facilitate post-test clinical management.[42] In a nation with a public health care system, there was less concern with preventing insurance companies from getting hold of genetic test results.

Defining the Roles of the Participants

As we can see, these regional BRCA testing systems configured the roles of participants in a very different manner than all of their counterparts in the USA. For example, the test providers at regional genetics clinics were much more tightly controlled by national and regional governmental authorities. The central NHS authority determined the territory covered by the regional genetics clinics, while the regional NHS authority determined the resources available to test providers.

Regional genetics clinics, however, maintained complete control over the allocation of resources and construction of testing systems. Thus, each had considerable influence over the roles of health care professionals and clients within its geographic jurisdiction. This led to regional variations in how the identities of users were framed. Genetics clinics that allowed open referral, for example, controlled only their own counseling and methods of laboratory analysis. They did not control health care professionals by requiring them to assess eligibility and restricting referrals, and clients could take the initiative to demand testing. Clinics that restricted access to high-risk clients not only managed their own counseling and laboratory activities, but also directed all health care professionals in a given region to refer only clients who exceeded a particular risk threshold. In such systems, both health care professionals and clients were tightly controlled. In contrast to Myriad's system, but similar to GIVF's, all clients who actually used laboratory analysis services at any regional genetics clinic throughout the UK also received genetic counseling from a trained specialist.

The UK: Developing a National Strategy

By the end of 1996, when BRCA testing services were available in most NHS regions, prominent UK clinicians and public health officials began to criticize the diversity of regional testing systems and advocate adoption of a national standard for BRCA testing. Many argued that regionally controlled systems did not support the NHS goal of providing every individual in the UK with equal access to the health care system.[43] They noted that the variety of testing systems led to 'a lot of inequity and uneven quality', with some systems being driven solely by patient demand while others had strict eligibility criteria for testing.[44] The variety in BRCA testing systems across the country, these critics feared, would provide NHS administrators with an excuse to reduce funding for both current and future genetics services – administrators could argue that genetics services were not provided to the UK citizenry in an equitable manner.[45]

This group of health care professionals proposed a national system that would provide UK citizens equal access to BRCA testing across the country. Whereas regional genetics clinics would still provide clinical care and laboratory services, the strategy for providing these services would be standardized across the country using a system of familial risk assessment and triage. The construction of the national strategy took place in three successive stages: (1) publication of the Calman–Hine report, which recommended that all cancer services be provided using a triage system; (2) publication of the Harper committee report, which proposed that genetic testing services should be limited to clients defined as high-risk; (3) development of a classificatory scheme that defined low-, moderate-, and high-risk categories and recommended services for clients in each category.

Using the Triage Method

In late 1994, the Chief Medical Officers of England and Wales, Kenneth Calman and Dierdre Hine, convened the Expert Advisory Group on Cancer to respond to a series of revelations in the early 1990s that linked high cancer mortality rates in the UK to poorly organized cancer care in the NHS (Hall, 1994a, 1994b; Rogers, 1994). The group published its report, 'A Policy Framework for Commissioning Cancer Services', in 1995, recommending the NHS to ensure that 'a patient, wherever he or she lives [will] be sure that the treatment and care received is of a uniformly high standard'. In addition, it suggested that cancer care would be provided through a triage system, a form of medical care familiar in the NHS (Calman & Hine, 1995). Three levels of care would be set up: primary care units (general practitioners); cancer units (for example, oncologists or breast surgeons); and specialist cancer centers (for example, where clients

could access research protocols). Each client would be channeled according to her or his specific need. Clients would be provided with equal access to the triage system, but the type of care they received would be determined by the diagnosis of primary care practitioners.

Cancer genetics professionals worked immediately to capitalize on the attention paid to cancer care by demonstrating how cancer genetics was an integral component of these services. Dr Peter Harper, head of medical genetics at the University of Wales, and a member of the Welsh regional genetics clinic, spoke to the report's authors immediately after its publication and strongly encouraged them to consider the role of genetic medicine in cancer services. Genetics could be easily integrated into their framework as a specialist service, he argued, in order to facilitate cancer prevention.[46] Calman and Hine responded by requesting Harper to form a committee to evaluate the relationship between the new genetics and cancer services. With funding from the Department of Health, Harper convened a committee composed of geneticists, oncologists, nurses, counselors, surgeons, a patient representative, and an economist to develop recommendations on how to integrate cancer genetics services into the Calman–Hine framework.

Defining a Candidate Group for Genetic Testing

The Harper committee finished its report, 'Genetics and Cancer Services', in December 1996 (Working Group of the Chief Medical Officer, 1996). It integrated its recommendations with those of the Calman–Hine committee, advocating the creation of a triage system for BRCA testing services. The first step of the system required physicians in primary care and cancer units to gather information about a client's family history of breast and/or ovarian cancer. A client deemed 'high-risk' according to their family history would be referred to the regional genetics clinic, which would serve the function of the 'specialist cancer center' as defined in the Calman–Hine report. While only 'high-risk' clients would be eligible for care at the regional genetics clinic, all clients could have a family history taken by a primary care practitioner or secondary level specialist and receive information about their genetic risk. The committee argued that the triage system would provide a clear mechanism to ensure that testing services were provided to the small fraction of clients who needed them rather than the large population who demanded them. In addition, they felt that this system would justify funding from the NHS by demonstrating a rational basis for the provision of services, as the system had similarities with other accepted cancer services that used a triage system to determine provision of care. 'There is a rapidly increasing demand for these services, and also for less well validated applications in lower risk situations for common cancers. Purchasers have until now lacked information on which activities are and are not of value, and there has been no clear mechanism for commissioning services' (Working Group of the Chief Medical Officer, 1996: 1). This move to develop a clear mechanism for commissioning BRCA testing services is not surprising. As Ashmore, Mulkay, and Pinch have described in their analysis of UK health care economists, development of rational standards to guide medicine is a recurrent theme in the NHS (Ashmore et al., 1990).

Interestingly, while the Harper committee recommended gatekeeping mechanisms that would standardize access to testing across the UK, it did not attempt to control the laboratory methods used to analyze the BRCA genes. It only noted, 'Laboratories undertaking presymptomatic genetic testing for familial cancers should be appropriately experienced and accredited, should be closely associated with clinical services in cancer genetics and should form part of the overall cancer center specialist services' (Working Group of the Chief Medical Officer, 1996: 3). Instead, the Harper committee adopted an approach similar to the regional testing systems and focused on the provision of counseling and testing: 'Presymptomatic genetic testing should be regarded as a process involving not only laboratory analysis, but provision of appropriate information to those requesting testing, as well as interpretation of any result in the light of all available clinical and genetic information' (Working Group of the Chief Medical Officer, 1996). In contrast to Myriad's system in the USA, the Harper committee sought to standardize how clients accessed testing and the type of care they received, rather than the laboratory methods that regional genetics clinics used.

Developing a Risk Categorization Scheme

The question of who fitted into the 'high-risk' category, however, remained. Soon after publication of the Harper report this issue was addressed by Dr James Mackay, an oncologist who headed the cancer genetics clinic at the University of Cambridge and had sat on the Harper committee, and by Dr Ron Zimmern, a surgeon and director of the NHS-funded UK Public Health Genetics Unit (UKPHGU). They defined low-, moderate-, and high-risk categories for the national classification and triage strategy, assigned eligibility criteria (using family history information), and articulated testing access and risk management options for each category.[47]

Like the Harper committee, Mackay and Zimmern proposed a national standard because they felt that genetics clinics would be unable to provide equal and appropriate care if they were overburdened with inappropriate referrals. One member of their team noted, 'If everybody went to regional genetic services, the genetic services would be swamped . . .. So what we are saying is, that . . . the categorization between low on the one hand and moderate and the high on the other, is really a categorization of who should be managed in primary care and who should be referred on'.[48] In contrast to Myriad's system, in which clients had the right to demand testing, Mackay and Zimmern saw demand as a problem they needed to solve. Mackay and Zimmern acknowledged, however, that the risk categorization scheme they had developed was based on limited research. At a

meeting with cancer genetics professionals, Zimmern noted, 'Today is not about art nor about science, but a mixture of the two. There is no good scientific evidence to guide us' (Mackay et al., 1997). The standard, however, would serve a very important purpose. It would provide an objective guide to deal with demand and justify triage.

A Client's Journey Through the National Testing System

In order to access this national BRCA testing system, a client visited a primary or secondary care professional who provided information about the BRCA genes and breast cancer risk and gathered information about the client's family history of breast and/or ovarian cancer.[49] Using this family history information, health care professionals classified clients into low-, moderate-, and high-risk categories according to Mackay and Zimmern's classification scheme.[50] If the client was deemed to be 'low-risk', she was reassured and turned away. If she was deemed to be 'moderate-risk', she could choose to go to the regional genetics clinic for additional counseling and possibly have access to a mammographic screening study. If the client was categorized as 'high-risk', she was offered access to the regional genetics clinic and laboratory analysis. Clients classified as 'high-risk' could also access specialized services such as increased mammography and prophylactic mastectomy without being tested. This interest in developing management strategies for both moderate- and high-risk clients demonstrated Mackay and Zimmern's, and more broadly the NHS's commitment to identifying all clients at increased risk of breast or ovarian cancer. Rather than focusing on identifying the small population of clients with BRCA gene mutations, as Myriad had done, proponents of the national standard were concerned with identifying and managing the larger population of clients at increased risk of breast or ovarian cancer.

Once at the regional genetics clinic, the moderate- or high-risk client typically met with a specialist in genetics and received counseling about the meaning of BRCA testing and its risks and benefits. If the high-risk client wanted to pursue laboratory analysis, one of her family members who had been affected by breast or ovarian cancer had to be tested first. Mackay and Zimmern argued that this would increase the likelihood that a mutation found in a family was linked to disease incidence.[51] If the family member consented to laboratory analysis of her BRCA genes, the health care professional sent her blood to the in-house laboratory. If she tested positive for a BRCA mutation, then the client originally interested in testing (as well as other family members) could be tested for the same mutation.

After laboratory analysis, the health care professional met with the client to present the results and discuss post-test management options. If she tested positive, she could continue to access preventive services. If a client tested negative for a BRCA mutation, however, she would lose access to these services. Results were then furnished to the primary care physician and, if relevant, to a specialist in order to determine the course of care.

Defining the Roles of the Participants

The UK national BRCA testing strategy framed the categories of both the client and the health care professional in a way that contrasted with that of Myriad, which had become the sole provider of testing in the USA. While Myriad defined health care professionals as facilitators who could help clients gain access to its testing services, the UK national BRCA testing system defined health care professionals as gatekeepers who would determine which clients could gain access to the genetics clinic and laboratory analysis services. These UK health care professionals were not the ultimate authorities in this testing system, however. Instead, health care professionals at regional genetics clinics and at the primary and secondary level simply implemented a strategy that had been developed by Mackay and Zimmern and other proponents of the national standard.

In stark contrast to Myriad, which defined a particular type of consumer who could not choose among testing systems but could demand access to any of the testing services that the company provided, the client in the UK national testing system was considered both a citizen and a patient. As a user of a government-run testing system, she was a citizen who was guaranteed access to the testing system, regardless of her ability to pay or of her geographic location. She also looked more like a traditional patient who could not demand a specific testing service, until being subjected to the risk assessment standards of the system and the clinical judgment of the health care professional.

Whereas, at first glance, it might seem as though the UK client was less empowered than her US counterpart because she could not demand access to specific testing and counseling services, it is important to complicate the definition of empowerment in two ways. First, as mentioned earlier, the idea that the right to demand access to genetic information is inherently empowering suggests that the client is perfectly informed and that having access to more information is automatically beneficial. In the case of BRCA testing, where the relationship between gene mutation and disease incidence is unclear, no 100% effective preventive, early detection, or treatment strategies exist, and clients often receive access to testing through primary care physicians who have no special training in genetics; information and choice do not necessarily improve decision-making. Second, the concept of empowerment in Myriad's system is clearly oriented towards the individual. In the UK, by contrast, the system and its notion of empowerment have societal as well as individual objectives. The national BRCA testing strategy was an attempt to find all individuals within the UK at-risk for breast cancer, and to provide them with the opportunity to manage their risk, while reassuring others who were deemed at lesser risk.

Conclusion

Through comparison of genetic testing for breast cancer in the USA and the UK, this paper has demonstrated how national political culture plays an important role in the architecture of a genetic testing technology. I have argued that, as providers in the USA and the UK began to build BRCA testing services, they not only navigated among existing legal and regulatory frameworks, but also adopted and adapted forms of biomedicine that were already present in each country. Understanding how social and political elements figure in the architectures of innovations can facilitate the social studies of technology in three ways. First, it provides a more detailed understanding of the factors influencing the development of technologies. We can see, for example, how OncorMed's effort to provide BRCA testing only through IRB-approved protocols not only highlighted its interest in integrating clinical care and laboratory analysis services, but also allowed the company to bolster the legitimacy of its system by relying on the existing credibility afforded to IRBs in the USA. Second, this approach helps identify persistent themes that may be relevant to a larger set of innovations. Acknowledging the recurrence of risk assessment and triage strategies in the UK health care can help us anticipate the types of tools available to the NHS as it introduces new technologies into its healthcare system. Third, it helps elucidate how more stable national norms and institutional frameworks shape the actions of groups immediately involved in the development of technologies. The shape of Myriad's BRCA testing service and its aggressive litigation strategy are not at all surprising in the context of the weak regulation of the clinical aspects of genetic testing and robust intellectual property regime in the USA.

This paper has also shown how the architectures of the BRCA testing systems built in the USA and the UK had important implications for the users of these services: shaping their roles, rights, responsibilities, and authority. In so doing, it highlights the subtleties of the identities of testing system participants. While the clients using GIVF's and Myriad's system might both be considered consumers because they received services in exchange for payment, their rights to demand services differed considerably. The client using GIVF's system had to receive counseling from one of the Institute's staff members, and could only access laboratory analysis of the three mutations common among the Ashkenazim. By contrast, the client in Myriad's system could choose among a range of laboratory analysis services and ask any physician to facilitate her access to testing. It is important to reiterate, however, that this apparent increase in consumer choice also meant that clients using Myriad's system did not necessarily receive the benefits of the clinical judgment of a trained specialist in genetics. Myriad's construction of a testing system highlights an important phenomenon in modern medical care: as individuals are increasingly encouraged to take charge of their own health care as a move towards empowerment, they are often assumed to be fully informed, independent, and confident decision-makers as well.

Finally, many commentators view BRCA testing – the first genetic testing technology for a common disease – as a test case that will guide how genomics is built into the provision of health care. If so, it is entirely possible that the architectures of the testing services that prevailed in the USA and the UK may become models for the development of future genetic testing technologies. In addition, the identities articulated in and through those architectures may extend beyond the particular systems to become more familiar as genomics is integrated more seamlessly into health care.

Notes

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1. Literature on comparative regulation has demonstrated differences in national policies related to science and technology, but this scholarship has left largely unexplored how national specificities influence the conduct of science and the development of technology (Vogel, 1986; Jasanoff, 1995; Gottweir, 1998).
2. Hans Klein and Daniel Kleinman (2002) have criticized SCOT's agency-centered approach, urging researchers to take the structural elements of societies into account.
3. This paper is based on fieldwork conducted from 1998 to 2001. I conducted in-depth, semi-structured interviews with approximately 100 individuals involved in the development of genetic testing for breast cancer in the USA and the UK. I used a snowball sampling methodology to identify potential interviewees, first interviewing individuals most visibly involved in the development of the new technology in the two countries and then relying on their referrals for subsequent interviewees. Interviewees included scientists involved in breast cancer genetics research, geneticists, counselors, and nurses who offered BRCA testing services to the public, innovators who developed BRCA testing, representatives of patient advocacy groups, government officials interested in regulating genetic testing, and scholars interested in the provision of genetic testing. I also analyzed documents provided by interviewees and reports produced by deliberative bodies concerned with the provision of BRCA testing. Finally, I attended meetings of the US Health and Human Services Secretary's Advisory Committee on Genetic Testing, the American Society of Human Genetics, the World Conference on Breast Cancer Advocacy, and the UK Genetics and Insurance Committee.
4. Throughout this paper, I refer to the person who engages with the testing system and is interested in having her blood analyzed for mutations in the BRCA genes not as the patient, but as the client. As we shall see later, testing systems sometimes defined the client as a patient, but also characterized her as a research subject, citizen, blood sample, consumer, or even a combination of two or three of these identities.
5. This attention to the roles, responsibility, and authority of participants in the BRCA testing system is built on scholarship by both Robert Kohler and Stephen Hilgartner, who have explored the moral economy of scientific practices (Kohler, 1994; Hilgartner, 2004).

6. While there were a few small providers of BRCA tests who served a very limited population during this period, the four US systems I describe in this paper were the most visible and successful.
7. In addition to being considered one of USA's best hospitals, the university's academic medical center ranked very high in monetary value of federal grants received (University of Pennsylvania, 2002a, 2002b).
8. US Geneticist no. 3. Personal interview, 21 March 2000.
9. Secretary's Advisory Committee on Genetic Testing (1999) *About SACGT*, 19 November 1999. Secretary's Advisory Committee on Genetic Testing. <http://www4.od.nih.gov/oba/sacgt/aboutsacgt.htm>, accessed 20 July 2001.
10. Public Law 100-578: Clinical Laboratory Improvement Amendments of 1988. 1988;42 USC 263a.
11. For more information on genetic counseling, see Hsia et al. (1979).
12. These forms functioned as what Susan Leigh Star and James Griesemer have called 'boundary objects', for they distilled the activities of the clinic – counseling, taking of family history, solicitation of consent – into entries on pieces of paper that would provide the laboratory with the information needed to conduct its analysis, including documentation for legal and ethical purposes and the individual's consent. Star and Griesemer write, 'Boundary objects are objects which are both plastic enough to adapt to local needs and the constraints of the several parties employing them, yet robust enough to maintain a common identity across sites.' According to Star and Griesemer's classification of boundary object types, the forms in GDL's system would be considered 'standardized forms': 'boundary objects devised as methods of common communication across dispersed work groups' (Star & Griesesmer, 1989).
13. In its 1995 Annual Report, the company stated: 'OncorMed provides a valuable linkage between new breakthroughs in cancer genetics and the research and technologies needed to translate these discoveries into diagnostic and therapeutic interventions . . .. We are the gene discoverer's link to one of the world's largest hereditary cancer databases. We are the innovator's link to clinical cancer genetics for promising new technologies, and the physician's link to some of the most sophisticated patient management tools available' (OncorMed Inc., 1995).
14. OncorMed applied for a patent on a consensus sequence of the BRCA1 gene. A consensus sequence is built by sequencing the BRCA1 genes of a number of individuals, and then at the most highly polymorphic (variable) points, averaging the most likely bases to be found at that location to create a full sequence.
15. Cancer Research Campaign and OncorMed (1997) *Code of Practice for Companies Seeking a Licence or Sub-Licence to the Diagnostic Rights of the BRCA2 Patent* (obtained from Cancer Research Campaign Technology representative).
16. US Geneticist no. 2 (1999). Personal interview, 11 January 2000.
17. The June 1991 *Federal Register* announcement is the only publication of the Common Rule (US Federal Register, 1991. *Federal Policy for the Protection of Human Subjects: Notices and Rules*, 56 Fed. Reg. 28002-28032, 18 June 1991).
18. 'Recently, we initiated our own IRB-approved national protocols for hereditary breast, ovarian, and colon cancers and familial melanoma, allowing us to broaden access to these services without compromising our high medical standards or commitment to patient protection' (OncorMed Inc., 1995).
19. The guidelines required that health care professionals gather certain information from the individual, including the subject's age, gender, ethnicity, and family history of breast or other cancers and outlined the type of information that the health care professional should provide to the individual interested in testing. They also required that health care professionals cover the following topics in the counseling session: information about the purpose of the test; the individual's option to be tested; benefits and risk of the test; sensitivity and relevance of possible results; clinical implications and limitations of results; possible psychological stress; who will have access to the results; relevance of the results to relatives and how to communicate such results to them; potential effects on health and life insurance policies; what will happen with the person's DNA sample; that consent is required before data are released to third parties; circumstances of release of non-BRCA2 data; such as gender of fetus and misattributed paternity (Cancer Research Campaign and OncorMed, 1997: *Code of Practice for Companies Seeking a Licence or Sub-Licence to the Diagnostic Rights of the BRCA2 Patent* (obtained from Cancer Research Campaign Technology representative).
20. PTT detects nonsense and frame-shift mutations (Buckley et al., 1999).
21. GIVF Institute representative (2000). Personal interview, 8 June 2000.
22. GIVF Institute (2001) Home. <http://www.givf.com>, accessed 9 October 2001.
23. Hadassah representative (2000). Personal interview, 13 July 2000.
24. Genzyme (2002) Main Homepage. <http://www.genzyme.com>, accessed 20 January 2003.
25. Recent scholarship in the field of science and technology studies, however, has highlighted the difficulties of defining human groups, and particularly, how defining the makeup of human groups takes place on a highly contested scientific and political terrain (Reardon, 2001).
26. Myriad Genetics Counselor (2000). Personal interview, 3 April 2000. Myriad employed people trained as genetics counselors to handle a variety of public education tasks, such as responding to enquiries from physicians and individuals about its testing services, discussing the testing service at national conferences of the American Society of Human Genetics and National Society of Genetic Counselors, and working with activists to allay their fears about testing.
27. Myriad Genetics, Inc. (1999) '. . . I did something new today to guard against cancer.' *New York Times Magazine*, September 1999.
28. Myriad Genetics, Inc. (2002) 'Myriad Genetics Launches Direct to Consumer Advertising for Breast Cancer Test.' Press release, 12 September 2002. Some scholars argue that such direct-to-consumer marketing practices have significant consequences for public understandings of illness and health. Tracing recent and current pharmaceutical marketing campaigns, Joseph Dumit demonstrates how bodies that were once considered healthy and only occasionally ill are now considered inherently ill on a permanent quest for good health (Dumit, 2003).
29. The company also furnished information about how to access specialized genetic counseling centers through its website. The website included a searchable database of 'Risk Assessment Centers' nationwide that offered 'genetic counseling and testing services to individuals at increased risk for hereditary breast and ovarian cancer' (Myriad Genetics Inc., 2000. Search for Genetic Counselling and Testing Centers. <http://www.myriad.com/gtpatbq2.html>, accessed 8 September 2000.) While the company did not want to become involved in determining the type of counseling that should be provided or the health care professional who would be in charge, it did provide access to such services.
30. These prices increased over time. While Comprehensive BRACAnalysis™ initially cost US$2400, for example, the price of testing was US$2600 in 2001. In addition, some states added charges to testing. In New York state, for example, BRACAnalysis™ cost US$2680 in 2000.
31. OncorMed also negotiated for, and received, licenses for the BRCA1 and BRCA2 genes from Mary-Claire King at the University of Washington and the UK Cancer Research Campaign. Myriad had filed for patents on its own research on BRCA1 and BRCA 2, while OncorMed supplemented patent applications on its own research (BRCA1 and BRCA2) with exclusive licenses on patents from Mary-Claire King's localization work and Mike Stratton's BRCA2 work. Myriad ran into problems with propriety when developing its intellectual property portfolio. NIH Director Harold Varmus threatened to file for a counter-patent on the BRCA1 gene when the company's initial patent application for the gene did not acknowledge as co-inventors NIH members of the Myriad team. They eventually settled the issue when NIH was provided with some license fees, the NIH researchers were listed as co-inventors on the patent, and the NIH abandoned its own patent application. The patent that was

eventually accepted subsequently was owned solely by Myriad (Associated Press [1994] 'Dispute Arises for Patent Over Gene', *New York Times* [30 October], section 1: 32).

32. Patricia Murphy, Antonette C. Allen, Christopher P. Alvares, Brenda S. Critz, Sheri J. Olson, Denise B. Schelter, Bin Zeng, OncorMed, Inc. (1997) *Consensus Sequence of the Human BRCA1 Gene.* 1997. US Pat. 5654155; Donna M. Shattuck-Eidens, Jacques Simard, Francine Durocher, Mitsuuru Emi, and Yuuke Nakamura, Myriad Genetics, Inc. (1997) *Linked Breast and Ovarian Cancer Susceptibility Gene.* 1997. US Pat. 5693473; Donna M. Shattuck-Eidens, Jacques Simard, Francine Durocher, Mitsuuru Emi, and Yuuke Nakamura, Myriad Genetics, Inc. (1998) *Linked Breast and Ovarian Cancer Susceptibility Gene.* 1998. US Pat. 570999; Mark H. Skolnick, David E. Goldgar, Yoshio Miki, Jeff Swenson, Alexander Kamb, Keith D. Harshman, Donna M. Shattuck-Eidens, Sean V. Tavtigian, Roger W. Wiseman, Andrew P. Futreal (1998) *17q-linked Breast and Ovarian Cancer Susceptibility Gene.* 1998. US Pat. 5710001.
33. US Geneticist no 2, 1999.
34. Myriad offered GIVF a deal: GIVF could continue to test for the three mutations common among the Ashkenazi Jewish population, as long as it provided Myriad with a fixed royalty payment per year. GIVF argued that it could not conduct enough tests to justify this payment, and shut down its testing service (GIVF Official, 2000). Some other small laboratories, such as the Memorial Sloan-Kettering Cancer Center, Boston University School of Medicine, and the University of California, San Francisco, did establish similar agreements with Myriad and continued to provide mutation analysis for the Ashkenazi Jewish panel (<www.GeneTests.org>).
35. Hockett, William A. (n.d.) Myriad Genetics, Inc. to Anonymous, University of Pennsylvania, 'I understand that you are currently providing diagnostic testing services for BRCA1,' Letter (obtained from researcher at the University of Pennsylvania).
36. Wight, Christopher L., Myriad Genetics, Inc. to Robert R. Terrell, University of Pennsylvania (1999): 'I acknowledge receipt of your letter of September 10, 1999, and appreciate your willingness to discuss and resolve this matter with Myriad.' Letter. 22 September 1999; US Geneticist no. 3, 2000.
37. Although private health insurance was widely available in the UK by the 1990s, no genetics services were available through private physicians in the UK. While some individuals chose to send their blood to Myriad's laboratories in the US for analysis, private insurance companies did not reimburse them for these costs.
38. UK Geneticist no. 1. Personal interview, 10 August 1999.
39. British Society of Human Genetics (2002) 'What Happens at a Medical Genetics Appointment?' <http:// www.bshg.org.uk/Patients/what_happens.htm>, accessed 15 October 2002.
40. The amount of funding that a regional genetics clinic received from the NHS to pay for BRCA testing services depended upon numerous factors, including the source from which the clinic was requesting the funding, the population of the region, and the existing expertise and infrastructure of the clinic. For example, regional genetics clinics used a variety of NHS sources to fund their efforts. Some clinics that had been involved in research to find the breast cancer genes reallocated this money to the development of BRCA testing services. Others requested additional funds from the regional NHS purchasers that were in charge of funding health care services for a particular region. A few appealed to the research and development section of the central NHS, proposing that the development of BRCA testing should be treated as an investigational venture rather than one with clear clinical benefits. In some cases, regional genetics clinics contracted with other laboratories to conduct the analysis of the BRCA genes.
41. Clinical Molecular Genetics Society (2003) 'Familial Breast Cancer.' <http:// www.cmgs.org/BPG/Guidelines/1st_ed/bc.htm>, accessed 10 January 2003.
42. UK Geneticist no. 4. Personal interview, 7 October 1999.
43. This effort to develop a national strategy for specialized services was not unique to BRCA testing. During 1998 and 1999, the NHS developed a consultation document for review by providers of specialized services across the country, in an attempt to 'renew the NHS as a genuinely national service. Patients will get fair access to consistently high quality, prompt, and accessible services right across the country' (The NHS Executive, 1998).
44. UK Geneticist no. 4, 1999.
45. Ibid.
46. Ibid.
47. The classification scheme also took into account the ethnic background of the individual interested in testing. If an individual was of Ashkenazi Jewish descent, she was usually automatically placed into the high-risk category and referred to the genetic clinic for counseling and testing.
48. UK Public Health Genetics Unit representative. Personal interview, 19 July 1999.
49. Mackay and Zimmern conducted a number of regional training seminars to ensure that these interactions would be standardized.
50. Some regions did not use the exact risk thresholds suggested by Mackay and Zimmern and outlined in their Table 3. While the exact risk thresholds may have varied slightly among regions, however, all regions used some type of risk assessment, classification, and triage scheme (Research and Development Office of the Anglia and Oxford NHS Executive and Unit for Public Health Genetics, 1998).
51. If the individual did not have any living family members who had been affected by either disease, she could not be tested.

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ABSTRACT Since the late 1980s, in France and in a number of other countries, cancer genetics testing has become a clinical reality, particularly for hereditary breast and ovarian cancer. BRCA tests allowing for the assessment of an increased cancer risk among patients and their healthy relatives are now being routinely performed as part of clinical practice. Based on fieldwork on French clinical cancer genetics and on the French Cancer Genetics Collaborative Network, this paper examines the configuration of entities, actors and activities mobilized by the performance of BRCA testing, and argues that the development of clinical molecular genetic practices is predicated upon the development of new forms of collaborative work that lead to a transformation of the content and organization of medical activities and judgements. The paper analyses three major collective configurations – local multidisciplinary collectives, data collectives and new clinical collectives – and argues that they not only provide the material conditions needed to carry out the relevant activities, but also articulate a series of distinctive bio-clinical interventions. These interventions provide an interface with research activities, produce the epidemiological measurements and tools that are a sine qua non for clinical work in this field, and, most importantly, establish the conventions that underlie practices, which define the criteria that turn tools and novel entities into operational components of clinical settings. It thus appears that in the field of clinical cancer genetics, bioclinical collectives, as a locus of expertise, have replaced the individual judgement of the practicing clinician.

Keywords breast cancer, clinical guidelines, family patient, French cancer genetics, genetic testing, medical work

BRCA Patients and Clinical Collectives:

New Configurations of Action in Cancer Genetics Practices

Pascale Bourret

The rapid evolution of molecular genetic technologies and the development of new genetic knowledge are expected to profoundly transform contemporary biomedical practices (Weatherall, 1985; Marteau & Richards, 1996; Conrad & Gabe, 1999; Cunningham-Burley & Boulton, 1999; Kaufert, 2000; Turney & Balmer, 2000). So far, however, the payoff of molecular genetics has been felt less in the therapeutic realm than in the diagnostic field. One of the most striking developments associated with the 'new genetics' has been the development of 'predictive medicine', that is, the use of DNA tests to predict the future occurrence of a given disease.

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