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SALVE REGINA UNIVERSITY

ATTITUDES OF
RHODE ISLAND PRIMARY CARE PHYSICIANS
TOWARD THE USE OF
GENETIC TESTING FOR BREAST CANCER

A DISSERTATION SUBMITTED TO
THE FACULTY OF THE DOCTORAL PROGRAM
IN CANDIDACY FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

BY
FRANCES M. ALEXAKOS

NEWPORT, RHODE ISLAND

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The dissertation of Frances M. Alexakos titled "Attitudes of Rhode Island Primary Care Physicians Toward the Use of Genetic Testing for Breast Cancer" submitted to the Humanities department in partial fulfillment of the requirements of the degree of Doctor of Philosophy in the Graduate School of Salve Regina University has been read and approved by the committee:

Reader: Frank D. Maguire PhD 3/31/03
Date

Reader: Thomas H. Brennan 3/28/03
Date

Mentor: Joan M. Cruickshank 3/27/03
Date

Vice President for Academic Affairs Thomas J. Maclennan 4-7-03
Date

ABSTRACT

Physicians currently consider genetic testing for breast cancer, especially the BRCA1 and BRCA2 tests, as problematic, because their predictive value, efficacy, and benefit to patients benefit vary greatly. Individual physicians are pressured by mounting patients demanding access to genetic testing. On the one hand, many patients believe that they have the right to know their future medical condition and that their physician is obligated to respond to this right. On the other hand, a number of physicians hesitate to offer genetic testing to patients because of ethical questions concerning the efficacy of the genetic testing, the psychological and social impact of such testing on the patients or their families, and the desire to honor a patient's rights to make his / her own decisions.

Additionally, legal issues surround the patient's perception of the physician's obligation to offer genetic testing. If a physician knows that a patient has a family history of breast cancer but does not offer the genetic test, and if the patient or a family member develops the disease, the doctor could be sued for wrongful practices. In brief, fear of possible legal suits and/or fear of patient reprisal can complicate the ethical questions that physicians must consider together to order BRCA1 and BRCA2 genetic testing for the prediction of breast cancer.

This study examined the attitudes of Rhode Island primary care physicians about ordering genetic testing for breast cancer. It also compared these attitudes with the gender and the length of medical experience of these primary care physicians. The research studied four attitude clusters: the use of genetic testing; confidentiality and a third party's right to know an individual's genetic information; the physician's feeling of competency in understanding the technological, ethical, legal, and social implications of genetic testing

for breast cancer; and finally, the attitude of physicians concerning responsibility to provide genetic counseling.

The results indicated that significant differences exist among physicians. Quite different attitudes were found regarding genetic testing and responsibility to counsel patients on the social, legal, and ethical ramifications of genetic testing for breast cancer. On the other hand, this study discovered no significant differences between physicians' gender or length of experience regarding patient confidentiality or adequacy of genetic technology.

As a result, these findings suggest a need to do further research on the differences found in this study. The question is, "Do these results reflect the attitudes of all primary care physicians or only the 162 doctors surveyed in Rhode Island?"

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I am grateful to my children: Alexis and Artemis, who helped to stuff surveys and stamp envelopes, and Katerina and Demetra, who helped to copy articles from the library. All four children spent many a night watching me at my computer and respected my need for quiet, uninterrupted time.

I thank God for the opportunity to research and for providing me with an understanding committee who helped refocus my attention on the details of the dissertation after the death of my husband.

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GLOSSARY

The following are definitions used in this dissertation. Unless otherwise noted, these definitions are adopted from Ricki Lewis in Human Genetics: Concepts and Applications (Boston: McGraw-Hill 1997, 403–11).

Akhkenaszi (m) refers to Jews of central and eastern Europe or their descendents as distinct from the Sephaxdron Jews of Spain, Portugal, or North Africa or their Descendants (From Webster's Unabridged Dictionary of the English Language New York New York: Random House, 2001;pp. 122 and 1746).

BRCA1 and BRCA2. The major genes involved in hereditary, early-onset breast cancer. The tests predict a level of risk for a disease that occurs in adulthood, and we do not know the appropriate medical interventions for women whose disease is attributed to mutations in the BRCA1 and BRCA2 genes (Collins 1996, 186-88).

Breast cancer. A disorder that results from a loss of cell cycle control, located within the tissue of the breast.

DNA. Short for deoxyribonucleic acid, DNA is the basic material of which our genes and genome are made. DNA resembles a twisted rope ladder. The side rails are composed of sugar and phosphate molecules, often called the backbone, and the rungs consist of base pairs (Golde 2001,1-2).

ELSI. The initials stand for the ethical, legal, and social implications of genetic testing.

Gatekeeper. The primary care physician in a managed care plan through who all other care (e.g., visits to specialists and other providers, lab and radiology tests, hospitalizations, etc.), with the exception of emergencies, must be coordinated. Such care includes genetic tests for breast cancer (Stanford University Medical Center 1996, 1-2).

Gender. The biological classifications of male and female.

Gene. A gene is a sequence of DNA that instructs a cell to produce a particular protein.

Genetic counseling. A medical specialty, whereby a counselor calculates the risk of recurrence of inherited diseases or disorders in families, using pedigree charts and applying the laws of inheritance. Goals include ensuring patient confidentiality, delivering information in a culturally sensitive manner, preserving patient

autonomy by delivering information in a nondirective way, and obtaining fully informed consent.

Genetics. The study of inherited variation and traits.

Genetic testing. This is a test of a person's genes, gene products, or chromosomes for abnormalities or deficiencies, including carrier status. Such abnormalities, which are linked to physical or mental disorders or impairments, may indicate the presence of or a susceptibility to illness, disease, impairment, or other disorders, whether physical or mental. These deficiencies may demonstrate genetic or chromosomal damage due to environmental factors (State of Rhode Island #97-H5157, 1997, 2).

Genome: The genome is a term for all the DNA in a living organism.

Genotype. Refers to the genes one inherits.

Health Maintenance Organization (HMO). HMOs are for-profit organized health care systems that are responsible for both the financing and the delivery of a broad range of comprehensive health services to an enrolled population (Stanford University Medical Center 1996,1).

Human Genome Project. A U.S. federal program that collaborated with scientists internationally to map and sequence the genetic makeup of humans. Numerous population screens, diagnostic tests, and therapies were examined in the project. An estimated of 30,000 gene markers were identified and sequences of the 3 billion chemical base pairs that make up human DNA were determined and were developed as a result of molecular biology and translated into easy-to-use biochemical assays, genetic tests, new drugs, and genetic therapies (U.S. Department of Energy 2002, 1-2).

Primary care. The coordinated, comprehensive, continuous health care that focuses on prevention and early detection of a disease and on maintenance of health.

Primary care physician. "All non-Federal doctors of medicine (M.D.) and doctors of osteopathy (D.O.) providing direct patient care who practice principally in one of the Four primary care specialties—the general or family practice, general internal medicine, pediatricians and obstetrics and gynecology—will be considered as Primary Care Physicians. Those physicians who engage solely in administration, research and teaching will be excluded" (Public Health Service 1993, 37).

CHAPTER 1

INTRODUCTION

Since the early 1980s, significant advances have been achieved in the field of medical science and technology. The Human Genome Project, begun in 1990, is an example of a major advancement in this area. A major goal of the project was to identify the estimated 30,000 genes in human DNA and to provide information regarding the genetic makeup of each individual. In addition, the project has the ability to identify variations in those genes that may lead to future illness (US Department Energy 1998, 1). "A working draft of the entire human genome sequence was announced in June 2000 and the analysis published in February 2001" (US Department Energy 2002, 1-2).

A genome is the entire DNA in an organism, including its genes. The sequences of genes in human DNA determine the makeup of each individual. DNA has been widely used by law enforcement agencies for purposes of identification of the assailant or the victim. We now have the ability to use this new technology to determine whether a person has a genetic condition that can predict the development of disease during his or her lifetime. Of primary importance to the present study is the development of a genetic test that can identify altered genes linked to breast cancer, called the BRCA1 and BRCA2. An individual who carries these altered genes may, at any time in the future, develop breast cancer.

In today's managed health care system, individuals seeking medical care generally rely on the primary care physician for medical treatment and advice. Consequently, the primary care physician has the responsibility to provide access to various diagnostic tests, including genetic testing for breast cancer (BRCA1 and

BRCA2). Because of its ability to predict the probability or possibility of disease in the future, genetic testing is fraught with more challenges than ordinary diagnostic testing. The doctor, who is responsible for determining the appropriateness of a genetic test for a patient, must be aware of the social, emotional, financial, legal, and ethical issues to which a patient and or physician will be exposed owing to the use of the genetic testing.

Ultimately, the physician must determine whether this new technology of genetic testing will benefit or harm the patient. If a physician decides that genetic testing would benefit the patient, then the doctor provides access to the genetic testing, communicates the results, and counsels the patient on the meaning of the test. Because the primary care physician may be asked about the use of the genetic test for breast cancer, the present study examines the attitudes of the primary care physician toward the use of genetic testing for breast cancer.

Statement of the Problem

Genetic testing to predict breast cancer by means of BRCA1 and BRCA2 is relatively new. In September 1994, scientist isolated a breast susceptibility gene, known as BRCA1, on chromosome 17q21 (National Breast Cancer Coalition 2002 b,1). Such tests are considered controversial by many physicians due to varying reports on the predictive value, efficacy and the benefit to patients. Even if found, the presence of the BRCA1 and BRCA2 gene does not confirm that an individual will develop breast cancer but only that she/he possesses the gene. The officials of the Human Genome Project and the National Cancer Institute, therefore, discourage widespread or public use of the BRCA1 and BRCA2 genetic test. Such officials recommend only clinical use of a genetic test that predicts a disease with a *proven* cure; where as breast cancer has no proven cure.

> Because nothing is known as of yet about the sensitivity, specificity and reliability of the genetic tests, and little is known about the effectiveness of genetic or psychosocial counseling in this context, genetic screening should only be available to individuals who agree to join peer reviewed, approved research protocols (National Cancer Institute 2002b, 2; Collins 1996, 186-188).

Nevertheless, there is growing pressure on physicians to provide their patients with access to genetic testing. Patients feel it is their right to know their possible future medical condition and that a physician has the duty to provide knowledge about possible or likely future diseases. Consequently, physicians often face a moral dilemma centering around uncertainty about the efficacy of the genetic test, concern about the psychosocial impact on the patients or their families after the results are learned and the desire to honor a patient's right to make his or her own decisions. Further, such ethical issues as informed consent, autonomy, beneficence, nonmaleficence, confidentiality and justice are additional factors that physicians must consider.

Legal issues surrounding informed consent are especially challenging. If a physician knows a patient has a family history of breast cancer but does not offer the genetic test, and if then a patient or a family member contracts the disease, the doctor could be sued for malpractice. Primary care physicians may also face an ethical dilemma when deciding whether to order a genetic test. These complex factors, particularly fear of possible legal suits or fear of a patient reprisal, add to the ethical dilemma facing physicians in Rhode Island and elsewhere over ordering a BRCA1 and BRCA2 genetic test for the prediction of breast cancer.

Background

The history of genetic technology began when in 1865 Gregor Mendel conceptualized the existence of the gene and demonstrated the principles of inheritance. Charles Darwin's work The Descent of Man (1871) theorized on the relationship between human inheritance and population. Darwin was credited with explaining the concept of how genetic mutation can impact a population. In 1933, Thomas Hunt Morgan, a United States geneticist, identified chromosomes as containing genes within their structure, hence establishing what Gregor Mendel had proposed in 1865.

The understanding of human genetics was significantly advanced in 1953 when two biophysicists, James D. Watson and Francis Crick, proposed the biochemical structure of DNA. In 1962, Crick, Watson and Maurice Wilkins shared the Nobel Prize for determining the "double helix" mechanism of protein synthesis. Furthermore, since 1968, an increasing number of genes have been located on specific chromosomes. Finally, in 1980, the technique of polymerase chain reaction (PCR) revolutionized genetic technology, allowing the understanding and copying of sequences of DNA at high rates.

This focus on comprehending the microbiology of all human genetic makeup by analyzing the human genome is the impetus of scientific exploration in the United States. Consequently, in 1990, the Department of Energy formed an alliance with the National Institutes of Health to spearhead an international, multidisciplinary, scientific venture called the Human Genome Project.

In that year, scientists involved in the Human Genome Project discovered that the BRCA1 is a large gene, located on chromosome 17 that contains 5,592 sub-units (Lalloo

1998, 10-12). The initial mutation found was located on 185delAG, which refers to a deletion of two of the sub-units of DNA (A and G at positions 185 and 186). In 1996, scientists found 100 places along the gene where alterations occur; by 1998, 200 mutations or alterations had been found in the BRCA 1 gene. A smaller gene, BRCA 2 has also been identified. The BRCA 1/2 genes, (breast cancer genes) when functioning properly, are thought to help suppress the growth of cancerous cells, while the presence of alterations, or mutations in these genes may be associated with an increased risk for developing breast cancer (National Breast Cancer Coalition 2002 a 1-4; National Cancer Institute 2002, 1-12.). These advances in understanding the function of the BRCA genes operate paved the way for testing to determine whether altered genes were present.

Twenty-first century medical technology, such as genetic testing, is expensive. This new molecular technology has facilitated the work of medical specialists who use this technology to study the human body so as to diagnose disease. Naturally, such specialists desire to examine patients. With managed care, however, medical costs are kept in check by using the primary care physician to serve as a gatekeeper to control medical specialist and expensive technology that is used for diagnosis of medical problems. In sum, primary care physicians are responsible for deciding which patients need and should have access to expensive, highly technical molecular genetic tests.

Developing Meanings of Technology

In the Information Age of the twenty-first century, technology shapes the way people make decisions, including medical decisions. The effects of technology on man have caused philosophers through the ages to reflect on its meaning. Aristotle's *Nicomachean Ethics* written in 336 B.C. considered technique, *techne*, as a skill, art, or