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Genetic Testing and Risk Classification

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Summary: Attendees are acquainted with the collision of issues that genetic testing is bringing to the insurance industry. Experts in genetics, risk classification, and state regulation present information and then participate in a lively discussion fueled in part by questions and comments from the floor. The following issues are explored, with a primary focus on individual life and health, disability, and long-term-care insurance:

- *What is the current state of predictive/diagnostic genetics?*
- *What laws that affect insurance have been passed or are being proposed?*
- *What ethical and discrimination issues are being raised?*
- *What are the potential solutions?*

Mr. Arnold A. Dicke: Our first speaker is Dr. Harry Ostrer, who is the director of the Human Genetics Program at New York University Medical Center. The Human Genetics Program at NYU is involved in research on human genetics and does

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genetic testing. Dr. Ostrer gets involved in genetic counseling and a wide range of topics that are of great interest to us. He'll be our first speaker.

J. Alexander Sandy Lowden is the vice president and chief medical director of Crown Life Insurance and a well-known speaker on this topic around the country. He has been at Crown Life for eight years. Prior to joining Crown Life he spent 25 years involved in biochemical genetics at Children's Hospital in Toronto, so he has some very hands-on information and exposure to this subject.

Robbie Meyer is the senior counsel for the ACLI and is a frequent speaker on this topic. Robbie is a native of Richmond and after running off to Tulane she came back up to the University of Richmond to get a law degree and worked at Life of Virginia and then went to the ACLI and has been there for 12 years.

Finally, the person who really is responsible for organizing this panel and has been doing a tremendous amount of work is Dave Christianson. Dave is a vice president at Lutheran Brotherhood where he heads up insurance services that includes underwriting and benefits, policyholder service, and insurance accounting. He has been there for 22 years, but from my point of view, a very important additional thing that Dave has taken on over the years has been a lot of work with the Academy. You might remember work that Dave did on the acquired immune deficiency syndrome (AIDS) study back in the 1980s. Now he heads the Academy's task force on genetic testing which is just about ready to put out an issue paper. You will receive it soon if you're an Academy member.

Dr. Harry Ostrer: I'm going to start off by telling you a little bit about the history of genetic testing. I had a very critical experience in 1975 when I was a medical student at Columbia. One of my classmates and I set up a genetic testing program for Tay-Sachs disease, which was our original prototype for genetic testing. Of course, at the same time Sandy Lowden was at a children's hospital in Toronto to set up his DNA testing.

Genetic testing has the ability to transform the practice of medicine as we know it. I'd really like to put it into perspective for you in terms of what we do now, how we do it, what we might do in the future and what some of the considerations are, especially with regard to the nonmedical uses of genetic information, which of course is of major interest to all of you. At NYU Medical Center the vast majority of testing that we do is carrier testing, some is DNA-based testing and prenatal diagnostic testing and an increasing fraction of our business is presymptomatic testing, especially for cancer risk.

Genetic testing is really used very little in the process of making medical diagnoses. Almost all medical diagnoses are made using conventional medical tools. I don't want to belabor these points too much in the interest of time, but even when there are unusual circumstances we know what medical tools that can help us sort out what's going on. An example would be the diagnosis of cystic fibrosis. When the gold standard test is normal or cannot be measured, we have a DNA-based test, although DNA is there to help us with making the diagnosis. For the child who is born with hypotonia, we have nonmedical tests, although the DNA-based test is there and is probably preferable right now in terms of what we do.

Once diagnosis has been made, genetic testing is useful for predicting recurrence risk. In a family in a which a child has been born with Duchenne's dystrophy, the common form of muscular dystrophy, about two-thirds of the time the mother is the carrier for that condition; about one-third of the time this is a new mutation that arises in the individual who has the condition. Of course, the mother will want to know if she is a carrier and whether she is at risk of having another child who is affected with this condition. Once we have knowledge about this, a very common reason for using DNA-based testing is for prenatal diagnosis, which may take a variety of different forms, depending upon what the specific condition happens to be.

Genetic testing, not surprisingly, is driven by the middle class. By and large we find that a patient's perception rather than a physician's recommendation is the driving force.

The prototype that I mentioned that we have for genetic testing was Tay-Sachs disease. Tay-Sachs disease is a progressive neurologic disease which, of course, is devastating to the parents of the children who develop it. It has been recognized for quite some time. In fact, there are certain populations in which Tay-Sachs occurs more frequently and one is Ashkenazi Jews.

Now in the early 1970s, two typical events occurred. First, the genetic basis of Tay-Sachs disease was identified and a carrier type was developed eventually in the late 1960s, but the second was that prenatal diagnosis became a possibility in the early 1970s through amniocentesis, and, as a result of that, Tay-Sachs screening programs were established around this country. One was established at NYU, which I inherited some time later, and one was established in Toronto. The incidence of Tay-Sachs disease plummeted worldwide. Remarkably, Tay-Sachs really became a nonjewish disease as a result of genetic screening. Some individuals still fall through the cracks because they don't have testing, their doctors don't recommend it, test results are misinterpreted, and so forth. There is still a measurable incidence

among nonjewish people. In fact, the thought that Tay-Sachs disease only occurs in Jewish people would be erroneous now.

In the early 1990s, genetic testing for a variety of other conditions became possible as well and among those conditions were cystic fibrosis, a pulmonary disease, and Gaucher's disease, a disease of the blood and the bones. In early 1994 we decided that we would extend the offering of genetic testing to the Ashkenazi community in New York for these conditions. New York has about two million of the ten million Ashkenazi Jews worldwide and therefore targeting genetic testing to our audience was an important thing to us.

The ability to do multi-type testing, and the ability to screen for other conditions was well received within this population. One group was tested for all three conditions, another group had been previously screened for Tay-Sachs, who now started screening for other conditions, and another group was screened for Tay-Sachs because that's what their doctor recommended. What we discovered as a result of our screening programs and demonstrated to others as well, was that each of these has a fairly high carrier rate and when you sum them up, the likelihood that an Ashkenazi Jewish person will be a carrier for at least one of them is approximately one in seven. This phenomenon is not unique to Ashkenazi Jews. Being carriers for recessive diseases occurs within other population groups as well. We just happen to know more about Ashkenazi Jewish people.

Of course the whole purpose of the program was to identify carrier couples and indeed to affect the reproductive choices of these individuals if, indeed, that's what they wanted. We found four carrier couples, two with cystic fibrosis. One went on to have an unaffected fetus and one went on to have an affected fetus. The next carrier couple had an unaffected fetus, and the Gaucher carrier couple had an unaffected fetus. In the past, these people would have only learned about their carrier status once they had an affected child, especially for Tay-Sachs disease, cystic fibrosis, and other conditions that have a measurable impact. People tended to stop having children once they have a child who was affected with a genetic disease.

One consequence of this program, of course, was that we also identified individuals who had the diseases. We anticipated this. Let me just remind you that for all of these diseases, you have to inherit two disease genes in order to be affected with the disease. There was one woman who had atypical cystic fibrosis and would have a lifetime of lung infections. She had been tested previously for cystic fibrosis and the results were always negative. There was one man with mild Gaucher's disease who reported that he had some bone pain several years prior to his testing. We offered him the possibility of a more extensive workup to see what the status of

his disease was, and he declined it because his wife was currently pregnant and he was concerned about the possibility of insurance discrimination.

Genetic testing must add value to patient care. What we find is that people do not choose genetic testing in the absence of a high prior probability. So having a family history of a particular disease or coming from a particular ethnic group is a driving force for people to have genetic testing. It's not just about Ashkenazi Jews, although we can add the following diseases to our list of recessive conditions within the Ashkenazi Jewish community Canavan's disease, Bloom syndrome, Fanconi anemia, Niemann-Pick disease, familial dysautonomia and what I just learned from the collaborator over the weekend, hereditary form of deafness. Among Dominicans we know of the condition called five-alpha reductase deficiency that results in abnormal sexual development among Puerto Ricans. We know of the condition called Hermansky-Pudlak syndrome, which is a condition of albinism. People from the Mediterranean basin, Africans, African-Americans, and people from Asia have very substantial risk for various blood disorders. All of these represent candidates for testing and much genetic testing is targeted to those specific groups.

As I mentioned a newer area of interest is that of disease predisposition, that is the inheritance of one or more genes that increases people's likelihood for developing specific conditions. At the time of testing, they are healthy. The one that has received the most press and probably the most work is cancer, but others on the list include hemochromatosis, an iron storage disease that affects the liver, the pancreas, the heart, and other organs; diabetes mellitus type I; and, coronary artery disease.

What we sometimes observe is that people who have hereditary predispositions to common diseases such as cancer have a family history. In a family that has a high incidence of breast cancer, the age of diagnosis is quite young for most of these individuals. Frequently the breast cancer may be bilateral and frequently the people may be at risk for development of ovarian cancer. It was from the identification of families such as these that susceptibility to certain diseases came to be identified.

Even in the absence of having a specific susceptibility gene or identifying the susceptibility gene within a given individual or family, we have empiric risks about what an individual's likelihood is for developing cancer over the course of a lifetime based on family history. If there is only one first-degree relative who developed cancer at an age greater than 50, the likelihood of that individual developing breast cancer is pretty similar to what it is in the population, about 9–11% or one in nine. By contrast, if there are two first-degree relatives, both of whom developed breast cancer at an age younger than 50, then the cumulative risk of developing breast cancer by age 80 is about 35–48% by time. It's never 100% and many people who

come to see us for genetic counseling about cancer risk really think that their histories are very loaded and they think that they're doomed. The genetic counseling experience alone can be quite reassuring to them. They might learn that there is a very reasonable likelihood that they will not go on to develop disease.

The reason that we know about genetic susceptibility to cancer is because cancer is a genetic disease and cancers result from a series of genetic alterations that accumulate in cells to go on to become cancerous. Some of these genetic alterations can be inherited from the parents, and some of them represent genetic alterations that occur within the tumor cells themselves.

With regard to disease susceptibility genes for cancer, we know of quite a number right now. Perhaps the most famous of these will be BRCA 1 and 2 which are the susceptibility genes for breast and ovarian cancer. We know four different genes that increase susceptibility for malignant melanoma one and two, and we also note susceptibility genes for rarer tumors including those of the thyroid, the brain for Hippel-Lindahl syndrome, Wilms' tumor, a kidney tumor in children, and retinoblastoma, a tumor of the eye.

Of course, all of these provide the possibility of performing genetic testing. What we find is that people will choose genetic testing if they perceive added value, even if it does not improve their longevity, or more directly, improve their quality of life. We're a bit more upbeat in terms of the possibilities of what we can offer people who have a positive test for susceptibility to cancer. I'll show you that in just a moment. In the circumstance of a predictive test for Huntington's disease, the British Columbia study reported that it had benefits for the psychological healthy persons who receive results that indicate either an increase or a decrease in their risk of inheriting the genes for the disease. What people find, I'm told, is it is intolerable to live with uncertainty. Even getting bad news is better than living with uncertainty.

Finally, in terms of my caveats, we also find that genetic testing is price sensitive. We have people who are willing to pay out of pocket for genetic testing. Fear of genetic discrimination is a driving force, and we also find that people are willing to sacrifice sensitivity for what it will cost. For instance, they're willing to pay for the cheaper, BRCA 1 and 2 tests that detect fewer mutations and take their chances.

We've moving to an era of brave new genetics, in which we'll be able to screen for 7,000 different diseases for which we know about genetic susceptibilities. These will have a variety of different patterns of inheritance. Some will be common; some will be rare. The quality of our tests will be fairly good, but not perfect. In turn,

we'll be able to use this information to tell people about things to avoid, how they might modify their diet, drugs they might take, and possibly even gene therapy.

Let's take a minute or two to consider what are we doing in the process, for instance, to identify a gene for cancer risk. First, we take the person who actually has the disease. Not surprisingly, they're the ones who are most informative to us. They tell us that this mutation is associated with this disease. If it's positive then we also test other family members. We tend not to recommend routine or random testing in the population, and we also tell patients that genetic testing is still investigational and that it's administered in the context of a clinical trial.

In terms of the process, we determine why people want to be tested and what they want to know. We obtain a detailed family history. We review medical records and pathology reports. We provide testing if it's appropriate, but testing isn't appropriate for everyone. People are frequently misinformed as well. People will call and say, "Gee, I want the colon cancer test," when what they really want is the breast cancer test. We provide a precise estimate with or without testing, and we inform them about methods of surveillance and/or prevention.

In terms of the benefits of genetic testing for breast cancer, if a woman has a negative result, you can provide her with reassurance. If she has a positive result, then we might advise her to increase surveillance and perhaps get into a discussion about accelerated childbearing. We might also talk about prophylactic surgery, such as removal of breasts or ovaries. We might also suggest that the woman may choose to decline hormone replacement therapy at menopause.

We believe that such information is best presented by medical geneticists or genetic counsel, although with the anticipated growth of genetic testing, we recognize that it will be moving into the mainstream of medicine. I personally don't believe that genetic testing should be provided by people who haven't had special training within the field.

Genetic testing isn't simple because it has implications for lots of different people. The question that always comes up is who should know? In terms of the individual, the questions that frequently come up are: Does that individual have not only the right to know, but a right not to know whether she is at increased risk for a specific disease? Or does she have a duty to know about that risk? Does the relative have a right to know? In New York State, for instance, we have an informed consent law in which we obtain informed consent from our patients. We can only disclose the results to other parties with the authorization of the person who has been tested.

There may be unrelated people who want to know the results of the genetic testing. The employer might want to know because of the implications for job performance or the cost of health care. Insurance companies may want to know because of the possibility of improved stratification in the risk classification process and, of course, much tighter concern about adverse selection. The state might want to know because the state has a traditional role in enumeration. The state is a major provider of health care benefits and the state has had a traditional role in promoting prevention of diseases.

The circumstances of children are quite special. Who decides when a child should have a genetic test? Typically what we use as a guide are, do the benefits outweigh the child's right to decide? We don't typically test a child for adult onset diseases; rather we defer that until their age of consent.

Genetic testing, of course, isn't only about disease susceptibility. My father had hazel eyes. My one daughter has hazel eyes like her grandfather whereas my other daughter has brown eyes like me. Eye color is not a simple trait, and we don't have a genetic test yet for eye color, although people might want to know. My brother had hazel eyes too so there is a bilateral inheritance of susceptibility to hazel eyes.

In the future we're going to be interested in genetic predispositions to other traits, including such traits as superior intelligence, superior athletic ability and even a predisposition to sociopathic behavior because such people may be unemployable, uninsurable and sequentially no one would want to marry these people.

Genetic testing has the greatest promise to our preventing the onset of disease in the future. I think that it will be the major public health initiative of the 21st century. Certainly that is a driving force for me as a medical geneticist but it is balanced by concerns for the potential for unfair discrimination, which I suspect some of my other panelists will be talking about. This is a much debated issue on both the local and national levels, and it has led to passage of a number of not always well-guided laws to attempt to regulate the use of genetic information.

Mr. Dicke: Do you have any reactions to this before we go on to the next panelist? I know there are some initiatives to produce a great deal of genetic information cheaply. For example, I've heard about a situation where microchips were being used directly to sequence genes, and so forth. What's the status of that? Is that likely to bear fruit in the near future?

Dr. Ostrer: I think there are two sort of general initiatives that we should talk about. On the one hand, there is an effort to identify all of the genes within the

genome and it's anticipated that, by the year 2005, we will have a complete sequence of the human genome. It has been fast-tracked a lot so we already have a good inclination about what parts of all of those genes happen to be. Of course, the identification of any new gene that has been linked to a trait provides us with the ability for developing a new genetic test. The other is improving genetic testing. Genetic diseases may be caused by many different sorts of changes that occur within an individual gene so a lot of emphasis has been placed on developing the methodology for testing for those different changes and that's what DNA is all about.

Mr. Dicke: Do they work yet?

Dr. Ostrer: They work quite well. They don't work great, but they work quite well.

Mr. Dicke: When we think about genetic things, we always think about inherited things, but actually a lot of components of various diseases, certainly cancer, are related to DNA and so forth. How do we make that distinction? Is it important to make it in this context at all?

Dr. Ostrer: I think that's another very important issue that you're raising. The genes have to operate in a vacuum. Environment influences can affect what genes do. In addition, because each of us has 50,000–100,000 different genes, when you shuffle the two halves of the deck together, we end up with unusual combinations in our offspring and our prediction of susceptibility based on inheritance of the single gene is limited. It is better for some conditions than for others.

Mr. Dicke: Will we find genetic tests used for conditions that are not entirely inherited? Are there any things out there or are these entirely for inherited gene conditions?

Dr. Ostrer: Another area that is getting a lot of medical interest, because it has a lot of importance, is drug metabolism and responsiveness to certain medications. Should you be taking the same medication at the same dose that I am taking for a disease that may lead to much more targeted types of therapies where we may be taking very different things for the exact same disease. Of course, this whole area of behavioral genetics has a lot of interest and has its proponents and detractors. If the insurance industry has been under a lot of heat about the issue of genetic testing, then the natural health researchers who are concerned about the genetic basis of mental illness and certain types of behaviors, such as sociopathic behaviors, have been very much under the gun as well.

From The Floor: You mentioned gene therapy. What's your feeling? How far away from that are we?

Dr. Ostrer: It's very difficult to do gene therapy well, and it is not surprising that gene therapists are finding that it tends to work best when a little bit goes a long way. As an example, there are certain gene therapy experiments that are being done now where viral genes are being given to people that improve the metabolism of certain drugs, making them more toxic. To treat certain tumors, the genes are being injected into these tumors. They are kind of innocuous when the drug has been administered to the person, but in the tumors the drug is now being metabolized at a very toxic level to kill the tumor cells. The key is a little bit goes a long way.

From The Floor: I know there has been a lot of work done, starting at the National Institute of Health. It has now continued on in California with regard to Gaucher's disease. There has been a significant amount of work done towards gene therapy. You still say that's a long way off?

Dr. Ostrer: The key to Gaucher's disease is that it is caused by the absence of an enzyme and the real success with Gaucher's disease was in identifying the enzyme initially and developing the ability to purify large amounts of that enzyme so that people with Gaucher's disease will get enzyme replacement therapy. Now the gene therapist for Gaucher's disease would like to be able to compete with enzyme replacement therapy, but, quite frankly, they have a long way to go.

Ms. Joan A. Hentschel: In all the diseases associated with the genes, are the genes mutually exclusive in the diseases that result. Are there any combinations of genes that result in certain diseases?

Dr. Ostrer: Yes. For an example, there are different susceptibility genes that we know of for cancer. The BRCA1 and the BRCA2 are distinct genes, yet mutations in both markedly increase a man's risk for developing breast cancer. There are other genes that likewise might increase people's risk for developing breast cancer.

Dr. J. Alexander Lowden: When I first came to Crown in 1990, I went to a meeting of the genetic testing committee of the medical section of the ACLI, and they thought that in about five years there would be a bunch of simple tests that we could use like the cholesterol and blood sugar tests of today that would be very highly predictive. These could give indications of life expectancy, and we'd be able to underwrite a lot better. I began at that point to try to dissuade people of those notions because it's really not going to happen that way. There are a bunch of other people who are trying to dissuade people who are concerned about genetic testing.

Some of them are listed here and almost all of these people have been saying no, except the ones down at the bottom who do things differently from everybody else. Even as we found out today, they number in different orders.

The real issue that triggers all the problems in genetic testing is discrimination and the word *unfair*. I was really pleased to see that because that has been a difficult fight to get people to consider discrimination as fair and unfair; however, that's what we do in underwriting. We discriminate and it's pretty important that we be able to discriminate. That's how we place our products. Discrimination is pejorative in most people's minds but it shows up all over the place.

In genetic testing, I think we will use a broad definition that includes all kinds of things, not just bits of DNA. Family history may or may not be in there, but I think the legislation that controls how we use genetic tests will be based largely on broad definitions.

Mr. Dicke: Sandy, just to be clear, you don't mean that we'll be prohibited necessarily from genetic testing in the broad definition? You just mean that genetic testing will be formed in those terms? If we want to be involved in the debate, we have to use the word the way everybody else uses it.

Mr. Lowden: I think that's true. There's no point in talking about genetic testing and saying I'm only talking about DNA if everybody else in the world is talking about something else.

There are different kinds of genetic mutations, and it's important to understand those that we sort of got close to a moment ago talking about the difference between germline mutations, which are the ones that you inherit from your parents, and somatic or acquired mutations, which happen to all of us as our DNA repairs and rebuilds itself constantly. As we get exposed to things in the environment, like cigarette smoke and all kinds of noxious vapors, we modify some of our own DNA and make mutations. So the end result in almost all of us is we have numbers of mutations that we didn't have when we were born. Some of those may end up causing disease.

Geneticists tend to classify diseases. Most of the disease that affect and are fatal to policyholders are multifactorial diseases. They have many different genes that are interacting with each other.

I want to talk about some autosomal dominant diseases because they're ones that get a lot of press. These are the diseases that people complain to legislators about. They want to know what will be done about the poor guy who has this bad gene?

They're ones that consumer activist groups like to talk about because their interest is in that particular single gene mutation. Most of the ones that affect adults are single gene mutations that cause all the noise, but the most of the ones that kill most of the people that we insure are multifactorial.

In a single gene mutation, everybody that has a nonmutant disease doesn't get the disease. It varies from one gene to another depending on the type of gene, but the percentage of people who get the disease have what is termed by geneticists as penetrants. Penetrants are a very important feature when you're looking at a gene and trying to underwrite it.

We look at dominant disorders, such as those diseases that are passed from your father to you and you can pass it on to your child. This is opposed to the diseases that need two genes, one from each parent to affect a child. The diseases Harry was talking about are mostly receptive diseases in which both parents have to carry a bad gene and they have one chance in four of passing it to their children. We don't see many of those in adult life, but we see lots of dominant ones in which a single gene is mutated. It usually doesn't produce disease until sometime in middle age after people made all the bad decisions like getting married and having children and buying a house and buying some insurance. Then they find they've got a disease that's going to kill them.

Let's look at three of these diseases. Let's first take Huntington's disease because every time I've ever been in a session where I've had to argue on behalf of the life insurer, the people on the other side of the bench are arguing about Huntington's disease. Huntington's disease occurs in about one in 3,000 people. It's an extremely rare disease. We only underwrite one a couple of times a year in our company. Most of the time this isn't really an issue, but it's a serious issue for people in those families because if your father had Huntington's disease, you have one chance in two of having Huntington's disease. If you have it, chances are you're going to be dead by the time you're 50 in a not very pleasant way. It's a neuromuscular degenerative disease in which you develop abnormal movements and dementia. It is a dreadful disease, but it's a very rare disease.

Harry referred to the breast cancer genes BRCA 1 and 2. You'll see lots of things in the press about breast cancer and these two genes. They don't cause so many cases of breast cancer, but they're there. There are also inherited colon cancers. The thing that's important about the latter two groups of disease is that you can do something about them. You can't do anything about Huntington's disease. If we know the risks we can make reasonable offers.

Let's look at Huntington's disease. It's autosomal dominant, meaning 50% of the offspring will have the disease. There is now a very good test called the restriction fragment length polymorphism RFLP test. This new test looks at repeat sequence in a particular gene, and it's a fairly specific test. You can tell very easily whether or not the person you're testing is going to develop the disease. But most of the people don't want to know that. A person by the name of Williams from British Columbia looked at about 1,000 people at risk for this disease and found that only about 40% of them wanted to know whether they would carry the gene or not. The other 60% didn't want to know the answer. These are only people who came to their clinic. So there are probably more people out there who didn't really want to know if they were going to get Huntington's disease. It's a dreadful disease and lots of people don't know.

Let's take an example of a 25-year-old man who's father had the disease. The father had the onset of the disease at age 35, and he died at age 50. His sister began to show signs at age 40, and she is currently age 45. There is another brother who is 38, who is symptom-free. He wants to buy a life insurance policy, and he doesn't want to have a test. What do we do with him?

Probably half the companies in this room would say, "No thanks, we can't insure you because the risk is too high. The a priori risk of developing the disease is 50%; there is a 50% risk that he'll be dead at age 50." He has about 10 or 15 years to go before he's going to get sick or before he's going to know whether he has the bad gene. Let's look at the years of life remaining in this man. If he has a bad gene, he's going to be dead at about age 50. In other words, he has 25 years left. Then if he doesn't have the gene, according to my life table, he's going to live to be about 79. Halfway between those two numbers is 39.5 years. If you take all the other things into consideration, including the lapsation and including the fact that you're going to get some antiselection in this group, since some of the people who you test, who say they don't know, will know, taking the halfway point is probably a reasonable risk judgment.

If you look up that risk in a table, it comes out to about 400%. You can rate something at 400%, but it's hard to sell. The other problem with it is that you would have to really insure the guy who doesn't have the gene at 400% for the rest of his life in order to make the thing work properly, and that's kind of hard to do. But you can put a flat extra on this person for 15 years before he is likely to know whether he has this gene or not, and you can sell a policy to him and to his brother who doesn't have the gene. I think that's kind of important.

Let's look at breast cancer mutations. About 10% of breast cancer mutations are caused by two genes—BRCA 1 and 2—and these make up about two-thirds of all

familial cancer. However, there are hundreds of mutations in two genes, so a simple test isn't very easy and this disease has variable penetrants.According to where the mutation is, the disease may or may not appear or may appear earlier or later in that woman's life. There is also big ethnic diversity in the distribution of those mutations.

In the early studies that were done, they looked at the risk of a woman developing breast cancer at various ages if she carried that gene. I took these figures and converted them into a measure of excess mortality making an assumption that about 25% of women who developed breast cancer with the mutation would die. I then converted that excess mortality and calculated out these figures for various ages. You can see that it drops off very rapidly. Of course the reason it drops off very rapidly is because in this age group the all-cause mortality for those women is high. There's a very sharp drop-off. The excess mortality of 450% is pretty difficult to underwrite. Those original studies were done in families in which there were three or more first-degree affected relatives—sisters, mothers, daughters.

Subsequently, a number of other studies have been done. One was done on Ashkenazi Jews, who, in addition to all those diseases Harry talked about, have an increased risk of having some mutations of BRCA 1 and 2. If you look at this as excess mortality, it is something you can easily underwrite so, to go around saying I shouldn't offer insurance to someone who has a BRCA mutation is probably wrong. Second, there is some evidence to show that if you do prophylactic surgery, you can probably cut that excess mortality in half. So we consider most of them over the age of 50 as having a standard risk. Those numbers are going to change. I think the important thing when looking at that is when one looks at some data on a mutation as a life risk, it's important to remember that data at this time are very slim. Hardly anybody has been tested and as more and more people are tested, those data will improve and change very rapidly. To start making hard decisions about who you will sell insurance to and who you won't sell to, on the basis of slim data, is a very difficult thing.

Colon cancer is another big killer. In fact, colon cancer is the second or third most common cause of cancer deaths in North America. There are several genes that are associated with colon cancer. The thing about colon cancer that's important is early diagnosis. There are three stages of tumor development. The tumor is local in the T stage; second it moves into the regional lymph nodes; and third it metastasizes all over the place. Once it metastasizes to bone cancer, your chances of survival are pretty low. If the cancer is diagnosed before the tumor has gone anywhere, your chances of survival are excellent. I think people who have a known mutation for a colon cancer gene, but have a colonoscopy on a regular basis, are a standard risk. I think the importance there is that colon cancer is a preventable disease and being

forewarned is forearmed. Those who know they have the gene is a value-added thing rather than something that puts them at a bigger risk. I think we're going to find that many of these kinds of gene tests will tell us something about that person. It will also tell that person about their own risks and how they can modify those risks by changing their environment or by increased perception.

The specter of genetic underwriting has initiated a lot of rhetoric, a lot of fear, and some terrible legislation. Most genetic diseases in adults are multifactorial, and no genetic test or simple group of tests is going to be able to tell us which those are. The semantic mutations, or the ones we acquire after birth, usually happen in tissue or an organ. They can't be easily tested, so we're not going to ever test those. Single gene disorders are very rare.

Harry talked about a whole lot of diseases that he thinks are fairly common, but none of you probably ever heard of any of them before because they're all pretty rare diseases.
There will be no value to test a mob of insurance applicants, but they can be underwritten and that's my real message.

Mr. Dicke: You said that you took the colon cancer risk with regular colonoscopy. Do you police that at all in some way?

Dr. Lowden: No, we don't.

Mr. Dicke: You just know people are in the habit of getting a colonoscopy?

Dr. Lowden: If you went through the trouble of having a genetic test to find out if you are carrying one of those mutations, you're probably going to have a colonoscopy. That requires some good genetic counseling, and perhaps some direction at the start, but I think most people would have one.

Dr. Ostrer: You said the genetic testing for Huntington's disease has been around since 1983. Why has it taken 14 years to come to the conclusion that it's possible to underwrite people with Huntington's disease? As it was in the past, many insurers really treated it as a no brainer. Huntington's was the classic model of the disease that you simply didn't underwrite.

Dr. Lowden: If you take someone who is 45 years of age who has not yet shown any signs, it's very difficult to underwrite that person. I took the guy who is 25 because you can make the numbers work. You can make them sort of work when he's 35, but after that, you have to wait. There are times when you can't underwrite someone with Huntington's disease, but Huntington's disease is a really rare disease.

It doesn't have any impact on the mortality statistics of any insurance company. Breast cancer is a common disease, and breast cancer has a national action plan. I think it's important to have a look at the numbers. When you look at the numbers, you can see that you can underwrite these diseases.

Mr. David J. Christianson: Sandy, there would be several companies that wouldn't underwrite for Huntington's. It's kind of all over the map?

Dr. Lowden: Yes. Send them to me.

Mr. Christianson: Could you comment quickly on hemochromatosis?

Dr. Lowden: If hemochromatosis is diagnosed before the person has severe involvement of the liver and pancreas, then the disease is a no brainer. The person can have regular phlebotomies and will have no problem at all.

Mr. Dicke: Phlebotomy means give some blood.

Dr. Lowden: Yes, they have to be bled.

Mr. Dicke: It is like what they did to George Washington? It probably was not for that disease.

Dr. Lowden: Yes, that's right—applying of leeches. This is a no risk of disease if the patients are properly managed.

Dr. Ostrer: The frequency in the population is about one in 400.

Dr. Lowden: Yes, it's much more common than Huntington's disease. It's a real disease. And many people who have no signs of hemochromatosis, other than having an affected family member, don't get insured, and they should, because this is a treatable disease.

Dr. Ostrer: As you know, Sandy, network television has had a field day with this. They get someone who has Huntington's disease or another condition, and they talk about how as a result of their genetic test, they've now been unfairly discriminated against. Of course, the insurance industry has really been left as the major heavy in all of this because of technical jargon about adverse selections and some of the other terms that are used. It has not carried a lot of weight with the public or with the legislators.

Mr. Dicke: We should probably move on to Robbie's presentation and get a little synopsis of the legislative status.

Ms. Roberta B. Meyer: I've been asked to give you a brief overview of the legislative environment in connection with genetic testing, both in the states and on Capitol Hill. As I'm sure you all know, this is a big deal to life insurers, disability income insurers, and long-term care insurers because much of this legislation can be construed to prohibit all medical underwriting by the insurance companies. It is subject to legislation, and the reason for this is because the legislation usually reads that certain insurers are prohibited from underwriting based on genetic tests, genetic information, and genetic characteristics. Often the definitions of those terms—genetic tests, genetic information or genetic characteristics—are so broad that someone looking at those definitions down the road could construe it to include essentially all medical tests or all medical information. As a result, this legislation could be construed to prohibit essentially all medical underwriting by the insurer subject to the legislation. Consequently, this could be construed to prohibit essentially all risk classification. As you all know, far better than I, this could have a tremendous impact on the current way in which life, disability income, and long-term-care insurers currently do business.

I'm going to focus all of my comments exclusively on life insurance, disability income insurance, and long-term-care insurance because those are the ones for which the ACLI has responsibility.

There has literally been an explosion of activity in 1997 in connection with genetic tests. We first saw the genetic testing legislation introduced in 1989 and 1991, and in each of those years there was one bill introduced. In 1992, we saw four or five bills introduced. In 1993 we saw about 15 bills introduced. In 1994 and 1995, there were about 30 bills introduced in each of those years in states throughout the country. This year we saw about 70 bills introduced in 31 jurisdictions across the country. President Clinton announced that he was very much opposed to health insurers being permitted to underwrite based on a genetic test in connection with health insurance, and he advocated legislation that would speak to underwriting for health insurance on the basis of genetic information.

Roughly eight to ten bills have been introduced on Capitol Hill in connection with this issue, but the real activities issue has been at the state level. Not only has this been a concern because of the sheer number of bills that have been introduced, which was more than double the number of bills introduced in previous years, but roughly half the bills, as introduced, sought to address underwriting for life insurance. Virtually all the bills sought to address underwriting for disability income insurance and long-term-care insurance. Virtually all the bills, as

introduced, contain broad definitions of genetic tests, genetic information or genetic characteristics. In other words, virtually all the bills could have been construed to prohibit essentially all medical underwriting by the insurers who were subject to the legislation.

In addition to this, in almost every jurisdiction where this legislation was introduced this year, the legislators who were pushing this legislation were very serious and really cared about this legislation. In the past we might have engaged in serious legislative disputes in three, four or five states. In 1997, the ACLI, with the help of its member companies, was actively involved in the legislative discussions in 24–26 states. Not only did we have a lot of bills, but we had a number of bills where underwriting for life, disability income, and long-term-care insurers was seriously jeopardized.

To give you a flavor of the breath of the challenge that we face this year, the states in which legislation was introduced included the following: Alabama, Arizona, Arkansas, Connecticut, Delaware, Florida, Hawaii, Illinois, Indiana, Iowa, Kansas, Louisiana, Maine, Maryland, Massachusetts, Michigan, Missouri, Nebraska, New Hampshire, New Mexico, New York, North Carolina, Puerto Rico, Rhode Island, South Carolina, Tennessee, Texas, Vermont, Washington, and Wisconsin. This year legislation was enacted in Alabama, Arizona, Connecticut, Florida, Hawaii, Illinois, Indiana, Kansas, Louisiana, Nevada, Tennessee, Texas, and North Carolina. In New York, they amended a bill that they had enacted in 1996.

This legislation is being enacted literally across the country, and depending upon how you look at it, we would characterize our results in most of these states as victories. In other words, we got long-term care, disability income, and life insurance typically exempted from the legislation or the legislation was committed to study the confidentiality requirements of these bills, which I haven't addressed at all to this point. They were adjusted so that they would not interfere with companies' ability to perform ordinary business functions.

Of greater concern to us this year than our victories were the losses. We are very concerned that the states in which we had losses are more reflective of the types of challenges that we should expect in the short term. The losses were in the states of Arizona and in Illinois, where legislation was enacted, which could be construed to limit underwriting, not only for medical expense insurance but also for disability income insurance and long-term-care insurance. In addition, statutes were enacted in Indiana and Alabama, which could be construed to limit underwriting for long-term-care insurance on the basis of genetic tests and genetic information.

As of the current time, there are 26 statutes on the books that deal with underwriting in connection with any form of insurance and on the basis of genetic tests or genetic information. What is most significant, from our standpoint, is none of the statutes enacted today prohibit underwriting for life insurance on the basis of a genetic test or genetic information. Three of the statutes, (in Arizona, Montana, and most recently, New Jersey), do require that if there is underwriting for life insurance on the basis of genetic tests or genetic information or genetic condition, and the underwriting action could have some rational relationship between the risk and the premium being charged, then they would say that there can't be unfair discrimination in underwriting on this basis. This is a standard that the ACLI strongly supports, and this is a practice that we believe companies adhere to in any event. There is no statute on the books that prohibits underwriting for life insurance on the basis of genetic information or genetic tests. Statutes are in effect now in Alabama, Arizona, California, Colorado, Florida, Georgia, Hawaii, Illinois, Indiana, Kansas, Louisiana, Maryland, Minnesota, Montana, Nevada, New Hampshire, New Jersey, New York, North Carolina, Ohio, Oregon, South Carolina, Tennessee, Texas, Virginia, and Wisconsin.

We continue to have concern about possible legislative activity this year, particularly in the state of Vermont, but also in the state of Massachusetts. The legislation in Vermont is unique and extremely troublesome. It has been passed by the first house of the legislature and this is the first piece of legislation that was crafted with the intent of regulating or limiting underwriting for life, disability income, and long-term-care insurance. As I'm sure most of you know, there is community rating for medical expense insurance in Vermont, so underwriting for medical expense insurance, which is typically the focus of this legislation, is of no concern in that state. So our lines are directly targeted. What is troublesome about this state is that life insurance lines are specifically targeted. No one is drawing a distinction between these three lines of insurance and medical expense insurance. There is a strongly held view that genetic tests are different and that underwriting on the basis of these tests should be limited. The bill in its current form, or in the form in which it has passed the first house, would permit insurers to continue to underwrite or brainstorm the results of existing information (in other words, the results of genetic tests that are in a proposed insurer's record when they come to apply for insurance). It would prohibit the ordering of genetic tests except under certain circumstances. Those circumstances would include situations where a test is ordered for calls or where a test measures the proposed insurer's current condition, unless the test is a genetic test as defined in the bill. It is a very complicated piece of legislation. We've had a number of our medical directors study this bill. The words of the bill are very difficult to understand. The definition of genetic test is very difficult to understand, and the exemptions from the definition of genetic test are very difficult to understand, which makes this piece of legislation not only

troublesome substantively (it is contrary to ACLI policy), but it's even more troublesome because, quite frankly, it's very difficult to know what the words mean or what they can be construed by a judge or a court to mean.

On a federal level, as I said before, President Clinton has announced his support for legislation that would prohibit the use of genetic testing or genetic information for underwriting health insurance. Eight bills have been introduced on Capitol Hill that would deal with underwriting. Only one of the eight, Joe Kennedy's bill, would seek to limit underwriting for life insurance and disability income insurance. The other seven bills are directed exclusively at underwriting for medical expense insurance. Six of the seven bills would amend the Health Insurance Portability and Accountability Act (HIPAA), the Health Care Reform act or the Kassebaum-Kennedy bill. That piece of legislation, which was enacted in 1996, takes disability income and long-term-care insurance explicitly out of its underwriting limitations.

For our purposes, this means that six of the seven bills introduced on Capitol Hill at this point would seek to govern underwriting for medical expense insurance only. The seventh bill would be the troublesome bill. That bill seeks to enact a new statute that would limit underwriting for health insurance and the definition for health insurance in that legislation is big enough so that it could possibly be construed to also include long-term-care and disability income insurance.

This is a new issue on the Hill. While it looks like the bills there are directed at medical expense insurance for the most part, it's really hard to say exactly where those bills are going to go and the direction the legislators are going to go with this issue. This is a tough issue. The science is very difficult for laymen. This is probably not as difficult for you as it is for most laymen. It is a very emotional, scary issue. It is a nonpartisan issue because every legislator that you talk to has a wife or daughter or a sister or a mother or a father who has had a genetic condition. It is beginning to be characterized as a woman's issue because of the test for the BRCA 1 and BRCA 2 genes. The breast cancer advocates are very articulate, very effective, and very sympathetic. Quite frankly, there is nothing you can say after a breast cancer survivor stands up and testifies. Risk classification and adverse selection is not a numbers issue. This is not a dollars and cents issue. This is about people. This is a very hard, scary, emotional issue.

Superimposed on this is the whole privacy issue. The Health Care Reform Act directed the Secretary of Health to develop recommendations with respect to the privacy of individually identifiable health insurance. The Secretary made these recommendations a month or so ago to Congress, and then Congress has two years in which to enact a very broad piece of legislation that would govern the privacy of essentially all personally identifiable health insurance. In addition, almost all

genetic testing underwriting bills have provisions that would deal with the ability to obtain, maintain and then redisclose the genetic information. It was unclear to us at this point whether or not we are going to see a free-standing privacy bill or privacy legislation attached to an underwriting bill, which incidentally on Capitol Hill is typically called the discrimination bill. Most people do not distinguish between fair and unfair discrimination. Privacy, too, as you all would expect is a very, very emotional issue. It is being fueled by a generalized fear of what might happen with someone's personal information. On top of that, people have a particular concern for and fear of that genetic information. We feel that this information is special, and it should be treated specially. Many people feel that no one other than doctors and researchers should be able to have access to this information. The issues of underwriting and privacy are intrinsically tied. As you know, if you can't get the information, you can't use it to underwrite and evaluate claims. The issues are both substantively and politically tied, and they're also very emotional issues. My thought for the next year or two is that we're going to have some very difficult times ahead of us just because this is a very difficult, hard issue.

Mr. Dicke: I think we better move right on and let Dave talk. I think his presentation relates directly to what Robbie just said.

Mr. Christianson: As Arnold told you earlier, I work with the AAA Task Force on Genetic Testing. We had hoped to have an issue brief for you on genetic testing. There is one out on risk classification that was published in February 1997, and that was just a primer on risk classification. We can't get out to help in the debate at each legislature, so we're going to put out issue briefs that are useable. There will be one on genetic testing in the next couple of weeks that will have a lot of what I'm going to talk about.

I just want to point out to you that the Academy has some strategic directions that really come into play to assess and prioritize key public policy issues, to gain some access to these policymakers, to provide some guidance in the areas of research, and to give some technical expertise. The Academy does not lobby for the insurance industry. It does provide information from an actuarial perspective, so you might see me diverging on some of my comments to what somebody else might say is pertinent to an insurance company.

I have spoken to many groups and what many outside groups have trouble with is the concept of risk classification in voluntary individual insurance. Many people think it's just a pooling of all the risks together. If you just have some good and bad and throw them altogether, things will be fine. That's more a description of social insurance and perhaps group insurance, but as I hope you all know, the purpose of individual insurance is to group similar risks having reasonably similar expectations

of loss. That's what we have tried to do in individual voluntary insurance because the choices are whether to buy, what to buy, how much to buy, and when to buy it. The insurance company doesn't have the right to look at what stage of health you're in. There can be some real antiselection problems that Harry referred to. I'm not going to go into antiselection at all because I trust each of you are somewhat schooled in that.

There are really two opposing issues. Why should people with genetic conditions be discriminated against? I haven't used the word unfair, but this is the way I hear the debate. Why shouldn't insurance be allowed to underwrite in the past? What's the matter with the way we've been doing it for all these years? I would like to insert that there are many real fears of discrimination but many of them are exaggerated. I would insert that insurers do need to underwrite to make voluntary individual insurance work. I think that there are solutions that can be developed that address both sides of the issues. In any case, much like what happened in the national health insurance debate, the various solutions that would come to play will have an impact on the entire public no matter which way this thing goes.

Let's discuss some of the fears that people express. "If insurers find out I have a genetic condition, will they cancel my coverage, or raise my premiums, or will I not be able to get future coverage?" As Robbie said, "Will they invade my privacy?" Privacy from the standpoint of the general public might be far different than what you consider it to be with respect to keeping the records private in an insurance company. The public is fearful that you will find out something about them in the underwriting process.

Insurance just wants a favorable risk. Will they exclude many from coverage? Will they cherry pick? Will I be forced to take genetic tests and find out information I don't want to know? Like Sandy said, many people don't want to know. Will people not seek out genetic tests because of insurance fears, and therefore not get the kind of help that Harry talked about. What effect will a test on one person have on another, especially offspring or siblings? If you look at these fears, you'll find that some are unfounded. You can't cancel coverage or raise premiums on individual voluntary life insurance. I don't think it's going to have a great effect on excluding people from coverage because, in the past, we have had many developments. Each time it has happened, we've come up with about the same number or about 4% being denied coverage. However, there are some things that people do have a legitimate worry about. Getting future coverage is one. Some might be denied in the future that wouldn't be denied today or might have a higher premium than they would today. In terms of finding out about medical records, insurers would still want to do that so privacy would be affected. We are finding that people aren't seeking out genetic tests. There have been articles written and

researchers are having trouble getting people to participate in their studies. It might not be happening to a great extent, but it's happening. People do have this worry about the effect this will have on one another.

There are issues that really make it hard to reach a consensus. There is a different idea of risk classification. Second, there is an issue between social fairness and what I would call economic fairness which is what actuaries tend to think about. Having 100% extra mortality doesn't mean you're sure to die from a certain disease; it just means you have a greater risk or there is a greater probability of developing the disease.

What's happening is each group is viewing itself in the rowboat, whether it's the insurer or the public, and each group views the other group as the shark. We probably need to get to a situation where we're working together on solutions.

Actuaries have traditionally looked at fairness in terms of economics because a fair price is one that matches your risk profile. The general public has that view sometimes, but they also have a different view that equality for everybody makes sense. Sometimes the general public wants to mix and match, and whatever kind of suits the person's situation tends to be how fairness is viewed. As you look at this debate that's going on, you can ask yourself what social view is being pursued? Is it a broad new view of insurance that says that everyone ought to be able to obtain insurance, and the risk factors should be ignored and insurance should be issued? It would have a very severe impact on voluntary insurance. I submit we've seen that happen in health insurance already, and you kind of know how that goes. It probably goes beyond genetic testing to anyone who is impaired. In other words, you start to get some fairness issues that say, how can somebody with a genetic predisposition to BRCA1 get insurance at standard rates, whereas somebody who has acquired something through the environment would not be able to obtain insurance or would have a higher rate? If you take the broader view, you'll believe that everybody should just get insurance, similar to the stand taken for national health insurance. If you take a more narrow view, you probably get a privileged subset of the genetically disadvantaged. This may be a growing group. It may grow, and it might eventually start to merge into the first group. So you really have to wonder what is the future of voluntary insurance.

We wonder if there is some middle ground that can be reached. Risk classification really does seem to be working fairly well today, but there are other people who really do have real fears and need some solutions. These are some things that our task force has looked at. There are some things that Sandy and Harry both talked about, so that doctors, insurers, and people being tested all understand the real mortality implications of this thing. Most people think that if they have a genetic

predisposition to something, they're going to get it and it's like a death sentence for them. That's really not very true at all. Many of these things have very little extra mortality implications, but if we could research these and take the more commonly talked about ones and get some real information, I think it could help a lot in the debate. Then these things could be translated into underwriting implications.

Second, if the issue really is a floor of protection for everybody, we could look at Social Security being expanded by raising the $255 benefit. No one is talking about expanding social security. They're talking about contracting it because of the cost structure; however, for very little money, the whole mechanism is set up, and if that's really the issue, it could be done.

Government high-risk pools exist in property and casualty insurance and health insurance in various forms. That is a possibility. Again, it might be expensive and you would have to figure out how you're going to fund it, but that's an area that could be looked at. One of the things that life insurance does carry is some tax advantages, and if you are denied, you would not have those advantages. I suppose you could find ways to have different tax designations for those, but I don't think our country is exactly going in that direction either.

Genetic insurance policies have been suggested. Before you sign up to take a genetic test, you would get this insurance policy that would give you guaranteed insurability. If everybody taking the test had to buy that insurance, perhaps that could be a mechanism for supplying a floor of protection. It would probably have to be one per person.

There are some industry solutions that are possible. High-risk coverages could be developed. Sandy talked about Huntington's disease. There are various diseases that carry the predisposition to die in 20 years. As an industry, we are issuing coverage to people who are 65, 70, 75, and even up to 80 or 85 years old. There are probably ways to develop products that could speak to some of these things.

Limited scope policies are possible. These are done more often in disability. Arnold asked Sandy about monitoring people for colon cancer. One of the things that is not done in life insurance but is done in property and casualty insurance is asking questions like, Do you have fire detectors in your house? Do you have airbags in your car? Perhaps there is some room for some things like that. If a person finds out about something and if they can demonstrate that they will keep up with their preventive measures, perhaps you could have some rating difference. These are all good possibilities that could be researched.

Then one other one that was looked at in the health insurance debate is some risk adjustment mechanisms that require some underwriting and some estimation of mortality so that the companies didn't get an unfair share of the extra amount at risk.

These are some solutions that we're talking about with the SOA Foundation. The Foundation could use your research dollars. Arnold and I were both talking with a number of the faculty and other interested people in Madison about some things that could be pursued.

I will conclude by saying I think there are real fears, but I think they're exaggerated and if we could get the word out to the general public about some of these, we could clear up some of those misconceptions. One of the things that I skipped by is that there are many coverages available for people right now who have some extra mortality. They can get guaranteed coverage.

I do believe that if we explore some of these other options, there may be some room for keeping the current system as it is today, and we could also take care of those who do have real fears about this.