Informal Discussion Transcript
Concurrent Session 2A: Drivers of Future Mortality

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ALLEN KLEIN: Good afternoon, and welcome to Session 2A, "Drivers of Longevity." Thank you for being here, rather than outside in the beautiful weather. I'm Al Klein, and I will be the moderator of the session as well as a speaker. I decided to introduce each of the speakers before they speak, so I will begin by introducing myself.

I'm a principal and consulting actuary with the suburban Chicago office of Milliman. My expertise is on mortality, longevity and underwriting. I'm primarily responsible for the life insurance industry studies that Milliman does, as well as I work on a lot of assignments related to my expertise. I'm involved in many different industry activities, both domestically and internationally. I am also a frequent speaker, both domestically and internationally as well. I received my bachelor of science degree in actuarial science and finance from the University of Illinois.

I'm going to start us off in the session and am going to talk about both past and future drivers of mortality and longevity. Our next speaker will be Laurie Orlov, who is going to talk about the technical drivers, and then Dr. Phil Smalley will talk about precision medicine. We will have time for questions at the end.

So I'm going to set the stage for us. When I think about mortality or longevity, I think that it's important to begin by looking backward and asking, What were the past drivers of mortality, and will they continue into the future? I've got three different past drivers here: decreases in infant mortality rates, traffic fatalities and smoking prevalence. I'm going to talk about the first two, as I want to spend the bulk of my time on the future drivers. The third one is here for your reference.

In terms of infant mortality rates, this graph shows a decline in infant mortality rates from 1990 to 2011 in the U.S. You can see it has decreased to a little over six. This second graph shows a number of different countries and their infant mortality rates in 2007. The U.S. is about third from the worst. If we fast-forward to 2010—this is from a CDC report—the infant mortality rate in the U.S. was 6.1 deaths per thousand, which was the fourth-highest rate among the 29 countries that were studied, more than double the rate of Finland and Japan at 2.3 and Portugal and Sweden at 2.5. So it looks like there's

room for improvement here. The reason I brought up infant mortality rates is I think this is one of the key drivers, in that if you save a life here, there is a potential of living 80 or more years, versus some of the other drivers, where you'll add 10 or 15 years to life.

Next is traffic fatality rates, and this graph shows—if you follow the black line, which represents all states—a decrease from about 15 deaths per 100,000 down to about 10 deaths per 100,000, moving from 2005 to 2014. And for an international perspective, I have Denmark and Canada. You can see a much lower traffic fatality rate of 3.4 deaths per 100,000 for Denmark in 2012.

Now, this isn't in my slides, but one thing to consider here is that in the U.S., the roads are much more crowded; there are a lot more cars, which is probably going to lead to a higher traffic fatality rate in the U.S. than most countries. Here are some other thoughts on it as well. There are some positives and negatives. For the positives, there are new safety features, including air bags, lane departure warnings, blind-spot indicator, reverse backup sensors, automatic braking. A lot of the cars on the road today don't have these features yet, so I think that we are going to save some lives as the newer cars with these features become more prevalent. Also, I believe there is less drinking while driving than we had in the past. Despite this, we still we have a lot of alcohol-related fatalities, but I think those have come down with the increased use of seat belts.

I don't know what's happened in other countries regarding this, but in the U.S., in order to get a driver's license, the new drivers need to spend a certain amount of time behind the wheel before they can get their license. So some states might require 25 hours or 50 hours. This is a pretty long time, so we should see some more safety from our younger drivers.

The downsides are texting while driving and increasing speed limits from where we were.

That gives you the kind of ideas and thoughts to help you estimate how these past drivers will influence the future.

Now I want to turn to the drivers of future longevity. What I'm going to talk

about is based on some preliminary work by the International Actuarial Association Mortality Working Group. We are putting together a paper called "Long-Term Drivers of Future Mortality," and I am chairing this work. We hope to finish the paper later this year.

I want to recognize the authors of the paper. We have 10 authors, representing seven different countries, so the paper should have a nice international flavor to it. The preliminary work we have done so far is to come up with our key drivers. You can see from the list that there are 11 drivers. I'm going to talk about each one in a minute. These are very broad drivers, so, for example, smoking was one I had mentioned earlier. However, you don't see it on the list here at all. The reason is that it would fall under the lifestyle driver. These are broad drivers, and our intent is to cover all kinds of issues related to each of them.

Before I start on the first driver, I want to provide you with some thoughts. There is a lot of overlap between the drivers. You might expect to see one specific driver in a particular broad driver, and it is not there. If this is the case, it will be in another broad driver, but you should be able to find it somewhere in the report. Many of the drivers have both a positive and negative aspect to them. I'm not going to focus on that too much in my limited time here, but you will see that in the report. What I'm about to present to you are my thoughts on each of these drivers. The paper may come out with something completely different when we complete it, as it will reflect the opinion of all of the authors, and the paper should provide a lot more detail than I'm certainly able to do in this limited amount of time. We hope that—although there are other papers out there on this topic—this is one of the most comprehensive papers on this topic.

All right, let's start with aging. You will see there is a little bit different shading on some of the topics. As I go through each broad driver, I am going to talk about all the drivers that are in green and skip over the ones that are in white.

The first driver is mental, physical and social activities. In all my work on older age and aging, if I have to be very succinct, the key to living longer is being active

mentally, physically and socially. There are a lot of aspects to this, but these are the really important items. Mentally, doing crossword puzzles, sudokus, other puzzles help to fight off Alzheimer's. Now, the science is not completely clear on this—that is, whether this will actually help—but I think it's worth doing these things to stay mentally active. In terms of physically active, you don't need to be running a marathon at age 80, but you do need to be active. Just walking is good for you; it has a lot of health benefits. Going out and gardening, moving around, just getting up and moving is what is really important here. In terms of social—friends, social clubs, religious groups—these are all important. I read something recently that said the number-one cause of death in the elderly is loneliness. I found that interesting, and social activities should keep the loneliness from happening.

There are a couple of other drivers on aging that I wanted to mention. The first is outlook. I just read an article that a positive outlook actually leads to a reduction in heart disease. I also think that, just in general, your outlook on life is going to influence your longevity.

Parabiosis is the other one I wanted to mention. This one could be under medical advances, but I've got it here, at least for now. This concept started back in the 1950s, and what they did was they took an old mouse and a young mouse, and they hooked them up—hooked them together by their bloodstreams. What they found was the older mouse actually became younger in every aspect. The younger mouse, on the other hand, actually became older. So fast-forward to today, where this is being looked at again. There is a company that was recently formed called Ambrosia. What they are doing is offering any healthy participant who is age 35 or older, to get a blood transfusion from someone who is 25 years or younger. Now, they are not going to hook up the bloodstreams and potentially make the younger person older, but they are offering a blood transfusion. This work is patient funded. The cost is $8,000. The person has to travel to Monterey, California, where this company is located, for the procedure. Ambrosia is going to keep track of these individuals over time and see if this procedure works, how often a blood

transfusion may be needed to maintain the younger age, etc.

The next broad driver is catastrophes. You know about most of these, but the one you may not be as familiar with is electromagnetic pulses, or EMPs. The last EMP that happened was in 1859, and we didn't have much in the way of electronics back then. What we did have was telegraph offices, and every one of them caught on fire from this EMP. EMPs come from the sun. It is just a huge electronic pulse. Now, EMPs are supposed to happen every 150 years or so, so we are due for another one. NASA predicted that they thought that there was a 12 percent chance of having one in the next 10 years; this prediction was as of 2015. If one does happen, it will be disastrous for us around the world. Many predict that we would go back to the Dark Ages if this were to happen, because everything is electronic now; all business connections, everything is electronic, so this could be a big problem.

Moving on to the next key driver—diseases. I want to talk about antibiotic drug-resistant infections. This is information from the U.S. in 2013. Overall, there were 2 million drug-resistant infections and 23,000 deaths. The three big ones were *C. diff.*, with 14,000 deaths; MRSA, with 11,000 deaths; and strep, with 7,000 deaths. The experts expect this to get worse as these infections are again becoming resistant to the antibiotics. The reason for this problem is the overuse of the antibiotics—you have probably heard that before—but another problem is that there are not a lot of new antibiotics in the pipeline right now. The reason for this is money. It's very expensive to do research and development for these antibiotics, and then once they are available, it is hard to make money because someone takes the antibiotic for 10 days, and then they are done. So there is not much money to be made. Again, there are a few new antibiotics in the pipeline, which is good, but probably not nearly enough that we are going to need.

One other thing I wanted to comment on about this on a more global basis is that tuberculosis is the most common infectious disease out there today. There were 9 million cases in 2013 and 1.5 million deaths worldwide.

The next driver is environmental. When we were deciding on the key drivers, we

initially came up with 18, and then we culled it down to the 11 we are now using. We used a voting approach, and this driver, environmental, was the only one that received a unanimous vote.

I am going to first talk about chemicals and hormones. You have fluoride and chlorine in water. You have perfluorinated compounds, which are nonstick compounds. Those can be found in stain-resistant clothing, carpets, dental floss, microwave popcorn, the take-away wrapper. You have phthalates, which are found in personal-care products like soap, shampoo, detergents; even toys have it in them. And you also have endocrine-disrupting chemicals, which are synthetic chemicals that either mimic or inhibit natural hormones. You can find these in pesticides, BPA with plastics, and in other industry chemicals. So what is the issue with all these? Well, they cause cancer and early puberty. As a matter of fact, in the U.S., now 16 percent of the girls reach puberty by age seven, and 30 percent by age eight, which is an incredible increase compared to what it was just a decade ago. What is wrong with early puberty? The experts say that it is likely to result in more breast cancer for women and in more prostate cancer for men.

Next is pesticides, and these have been found to cause Parkinson's disease and cancer.

Pollution. According to the World Health Organization, there were 7 million deaths worldwide from air pollution in 2012, and according to the Environmental Protection Agency, indoor air pollution is up to five times worse than outdoor air pollution. Indoors you have volatile organic compounds, which are gases from things like fingernail polish, paints, paint thinners, air fresheners, as well as some of those other things that I mentioned earlier. These cause respiratory problems, cancer and birth defects.

Now, let's move to health care and medical care. The number-three leading cause of death in the U.S. is medical error. Phil is going to talk more about this, so that is all I'm going to say on it. The U.S. health care system ranked worst among 12 developing countries according to the Commonwealth Fund. The U.K. was number one, and

Switzerland number two. The other countries involved were Canada, Denmark, France, Germany, Japan, the Netherlands, Norway and Sweden. The U.S. system was the most expensive and had the lowest rating in terms of both efficiency and outcomes. I have also read a couple of articles about some bad doctors who don't follow good practices and yet they get to continue to practice without reprimand or additional education.

Inequality is the next broad driver. I want to talk about socioeconomic differences here. I have a number of different maps from around the world, showing differences in mortality by region within many different countries. This first one is probably my favorite. It shows the London Tube map and the life expectancy at birth at each London Tube stop, as well as child poverty. The darker the gray, the more poverty there is. You can see that generally there is lower life expectancy in the areas with more poverty. The other thing that I found interesting on this is just two Tube stops away—from Leicester Square, with a life expectancy of 90, to Holborn, with a life expectancy of 79—you have an 11-year difference in life expectancy. Again, just two Tube stops away.

Next, I want to show something similar within the U.S. This first map shows mortality in the U.S. by region. You can see in the south, a little bit to the north, and some areas in in the west have higher levels of mortality. This next map, which was created independently, is not a perfect overlay, but it still shows that higher poverty levels in the U.S. are in about the same places as the higher mortality on the previous map.

Education levels, similarly, are lower in the south, a little bit to the north, and somewhat in the west. Again, it is not a perfect overlay, but there is a lot of correlation between this, the next map on violent-crime rates, and the original map on mortality by region. Therefore, poverty, education level, and violent-crime rates are probably some of the reasons for these differences in mortality.

Next is lifestyle. I want to start with diet and nutrition. We all know that diet and nutrition are important, but the question is, Do we really know what is right or what is better for you? I am just going to touch on a couple of things here. First, I am going to say that fat is actually good for you and sugar is bad for you, which some of you may

know but some of you may not. When I say fat is good for you, I am talking about saturated fat. Sweden did a two-year study on saturated fat, and in 2013 added it to their dietary guidelines. They indicated that not only is it not going to cause you to get fat, but it may actually help you lose weight. Now, I'm not telling you to go out and eat 10 sticks of butter; moderation is important. But I wanted to let you know that it is good for you. What is not good for you from a fat standpoint are the man-made fats like trans fat. Sugar is not good. High-fructose corn syrup is considered a sugar and is one of the leading causes of obesity, in addition to the previously mentioned chemicals and hormones.

One other one item I wanted to mention is that I used to drink skim milk for many years. However, what I found out not too long ago was what they do when they make skim milk. They take the fat out, which I just told you is good for you, but they also take out nutrients, and they replace it all with sugar. So skim milk was not the way to go; it is not better for you.

Next, I want to talk about exercise, and again, do we know what is really good for you? I was reading a couple of articles recently that say that jogging actually ages you and is not good for you, but what is good for you is interval training. So a fast burst, rest and then do it again—that is really the best exercise for you. Now, if you have not exercised recently, do not go out and try to do this without building up to it.

I mentioned what causes obesity, but the results of obesity with respect to mortality and longevity are unknown so far. Sam Gutterman put together a good paper on this topic. It talks about the different aspects of obesity, but I do not know if it has been published yet. My opinion on obesity is that we are going to see people dying more frequently in their 50s and 60s, rather than their 70s and 80s.

The last lifestyle driver I want to discuss is stress. Stress leads to chronic inflammation, more heart disease, stroke and maybe Alzheimer's as well. We are all under a lot of stress, so those who can better control it will likely live longer. Stress is a big killer.

Medical advances. I am going to spend more time on this key driver. The first

driver I want to cover is 3D organ printing. I believe they can now make an exact copy of a replica of a person's organ. What they do is, instead of printing with ink, they print with biomaterials to form that organ. I am not exactly sure where scientists are in this process, but I believe if it is not yet available, it is very close.Bioelectronics is using electronics for healing.

CRISPR stands for clustered regularly interspaced short palindromic repeats. What does that mean? For those not familiar with CRISPR, what it does is it allows for the replacement or deletion of specific genes. Some examples of where it could be used include deleting embryonic genes known to cause health problems, editing immune-system cells to better fight cancer and changing things like soybean oil, which is a trans fat, into something where it is closer to olive oil, which would be good for you. There are many exciting uses here. While CRISPR has already been used, it is really just getting started. While I believe there are many potential great benefits of this technology, my concern is on any unintended consequences that might show up.

I want to touch on genetics briefly. What a lot of people don't realize is when you have a genetic test, it will also tell you what drugs will work for you or won't work for you. So this could be very valuable in creating more appropriate treatments geared toward the specific individual and their issues.

Immunotherapy. The way cancer works is that it fools the immune system so that the immune system doesn't realize the cancer is there and therefore does not attack the cancer. Immunotherapy drugs help the immune system recognize the cancer and attack it—generally, in early results, completely wiping it out. Jimmy Carter has been cured from his cancer, and others have as well, using immunotherapy. However, within the past week, I just read that there is a potential downside to this, and that is for some individuals, after they got their cancer cured, the immune system kept attacking their body after that and actually killed them within two years of ridding the body of the cancer. So there is still some work to be done, but I think this treatment is very promising; it just has not been perfected yet.

Telomeres. These are enzymes at the end of every chromosome. They shorten with each cell division. The length of the telomere is said to be predictive of biological age. Not everyone is convinced of this yet, but some do believe it, and they are discovering ways to lengthen telomeres as well, which would hopefully lead to longer life.

I just came across a study by Northwestern Medicine and Harvard University that discovered that cancer can be predicted years before it happens, following a certain pattern of telomeres. The pattern is found over a period of time. What they found was if telomeres decrease rapidly for a period of time, such that the person is 15 years older than their actual age, and then suddenly the decreasing slows down and actually stops for three or four years, after that time, cancer shows up. I found this really interesting, that they were able to find this.

The next key driver is political. I think what is important here is whether regulations will inhibit or promote further research that is needed. Also, will there be enough funding and resources for safety issues; more open space and green space, which is considered to be healthy for the population; and for medical research?

Next are technological advances, and I will talk about a few here. First are ingestible sensors. These can be taken either with pills or incorporated into medicines. Once they are swallowed, they get activated by stomach acid, and what happens is the stomach acid relays the message to a patch that you wear, which looks like a Band-Aid, and then from that patch, information gets relayed onto either a smartphone or some other source that is monitoring this. What is monitored? It could be either medical adherence or measurement of vital signs like heart rate and temperature.

The Internet of things. This is either sensors or computers talking to one another. Ingestible sensors are one example. Another example is having a sensor in the home of someone who is elderly. It may measure, for example, that they turn on their coffeepot every day at about six in the morning for weeks. Now all of a sudden, for two days in a row, they are turning it on at two in the morning. A signal can be sent to the children or

somebody else that lets them know that there might be something wrong.

Robotics. Exoskeletons have been created to help people with spinal injuries to walk again. This is a recent advancement. There also robotics for the elderly, which can help them keep appointments, remind them of appointments, keep their attention. If the elderly person is feeling sad, the robot can play their favorite song. It can also potentially help pick them up if they fall. These are more common in Japan than elsewhere around the world, but they are coming.

Self-driving cars. I have seen some examples—actually, videos of self-driving cars—where at an intersection you have cars that don't slow down and also never get into an accident. This would allow cars to be really efficient, not stop, and traffic can be controlled. This could be a good thing! The one downside that I am concerned about is the hackability of these cars, because a lot of the electronics that are out there right now and continue to come out are still very hackable. We don't want someone sitting up on a hill above a busy intersection to have the ability to program trouble for the helpless drivers.

To finish up here, the last key driver in our list is what we don't know today. These could include disasters, ongoing research, new technologies, travel, knowledge, nanoparticles, outer space, work environment—and there are many other places where new things can come from. I want to mention a couple. One is could we use virtual reality if there is an emergency in the home to tell you what to do and how to treat it. I don't know if that is currently available; I don't think it is, but I don't know for sure. Another one is having babies created from three sets of DNA instead of the normal two. This actually has started happening. The U.K. has just approved it, and while the U.S. has not approved it, some U.S. scientists went to Mexico and actually did this.

That is all my prepared comments on my topic, so thank you for your attention. Please save your questions for all of us until the end. I am going to introduce Laurie and then let her speak.

Laurie Orlov is a tech industry veteran, writer, speaker, and elder-care advocate.

She's the founder of Aging in Place Technology Watch, a market research consultancy about technologies for older adults. Laurie has spoken regularly and delivered keynote speeches at forums and industry conferences, most recently on the business of technology for boomers and seniors. She advises large organizations as well as nonprofits and entrepreneurs about trends and opportunities in the age-related technology market.

Laurie has a graduate certification in geriatric-care management from the University of Florida and a B.A. in music from the University of Rochester. Please welcome Laurie.

LAURIE ORLOV: Hello. So I'm just going to tell you a little bit about myself, and I'm going to provide a little bit of context for the comments I'm going to make about the technology market, because I am a market industry analyst. I don't predict so much about the future as I track what's going on in the present and what's about to happen in the technology space. This is a very exciting week, by the way, in the technology industry. I'm not sure you're familiar with it, but the Consumer Electronics Show begins tomorrow, and that is going to have 170,000 people from around the world, and this is the show every year in which new technologies are introduced into the marketplace. Whether they stick or not is subject to price and general market interest, but the technology market is changing very rapidly, and this is exactly what I do. I've been doing it for many years, specifically in aging for the past seven or so years I've been looking at those.

So I'm going to give you my context about this topic, which is maybe not always the common statistics you might hear. Some of them actually are from the Society of Actuaries, though, so hopefully they match what you know.

So I see that there are 46 million people 65-plus, but I'm not so interested in them. I'm more interested in the population that's aged 75-plus, for which there are 20 million, and the population that's 85+, for which there are more than 5 million, and particularly the average age moving into assisted living these days is now around 85. The average age in assisted living is 87. They are mostly women, and one of the Society of Actuaries numbers that I quote at speeches that I give I think is really compelling, and that's the

longevity at 65. Not longevity at birth, but one if you make it to 65, women are going to live to an average of 88.8, and men 86.6. And if you couple that with the fact that 46 percent of women aged 75-plus live alone and that if you look on the far side of those averages, there's going to be a lot of women living alone, and they're not going to be in assisted living because of the deferred move-in date and I'll get to that in a second about the price, so they're going to be in their own homes.

So one of the things to think about in this context is—as I said, I'm more interested in what I call the real seniors, and the real seniors are the ones who are aged 75-plus—and the question is, How can technology be helpful in connecting what I see on the right side as the informal network of family and payers and on the left side the providers, which could include doctors, geriatric-care managers, home care workers, assisted-living facility staff, skilled-nursing facility staff? And I would like to fill in the lines on this triangle and say that these groups are well connected. They are more connected now than they were when I first started tracking this space seven years ago. But a prediction was made at that time by one of my colleagues in the space, and he said, "Before the tech revolution, the village took care of you, and now we will have an electronic village." And the question is, Are we there yet? Do we have an electronic village? Do you feel that the older people that you know about actually are in an electronic village, or are they simply in a village?

Mobile Health News predicted this past August that there was going to be an incredible adoption of wearable devices by 2018, a very high percentage of use by seniors, but do you see that? Do you see a high percentage of wearable devices on seniors, and do you think this market is really moving right along? I would say it has reasons for us to believe that it's, in fact, not moving right along—that adoption begins in these spaces in terms of wearables, but then people get tired of them, and they abandon them largely because they're not connected to anything else that's really useful, that helps the quality of their life.

So if we look, the reason why technology has such an interesting role to play in

our future aging lives really has to do with the costs and population associated in this chart. And if you look at the bottom left-hand corner of this graph and you look at the fact that in 2016 the median cost of assisted living in the United States was $44,000 a year, it's projected that it will be $51,000 a year by 2020 in the United States, and then in some regions right now, $51,000 has been exceeded. And I'll just give you a small example of my own mother-in-law, who is 93. She's in a dementia unit in assisted living, and her costs are now $66,000 a year, and she's in one of the lowest-cost parts of the United States, which is Florida. So in some regions, it's well more than that to live in a dementia unit in assisted living, and people move into dementia units when they can sell a house and can afford it. They move in because of the level of care; they are wander risks, they no longer have skills of communicating. But where is the cost of that care headed in the future? It means really that assisted living is not going to be affordable for most people in the United States, and in fact, the gaps in the growth and the cost of care, the price of assisted living and the population [are] the opportunity for the use of technology moving forward.

This is another chart that's kind of a shocker, really, when you think about the context of lifestyle and capability of older adults. This is the median net worth of Americans, and the blue is net worth, and the red is next worth excluding equity in your own home. And the interesting number here is the median net worth of adults aged 75-plus, inclusive of their home equity, is $156,000. Now you see why they're not moving into assisted living. They can't afford it, and boomers are worse off. Their age retirement portfolio is $136,000, and so what that means is that boomers are going to stay home. The oldest boomer right now is 70. Boomers are going to stay home rather than move into assisted living. They may move in with their children; they may move into group housing, what's called co-housing. They may have a wide variety of strategies, but right now, the assisted-living industry is not prepared to cope with a population that has a net worth that is what you see there.

So taking another look of this view of care, in 2013, AARP published a very

interesting report that was about the growing caregiver support ratio problem that would reveal itself by 2030. What they said was there were seven people in the age ranges of 46 to 64 available to care for the population age 80-plus, and that was in the year 2013. And what they said was, by 2030 there would only be four people in the ages of 46 to 64. Now, that is independent of whether those people are your family members, your home care workers, staff in a particular geography of service providers. So we took a look at that, and we looked at the fact that all care is actually local, and so we took a look by county in the United States, and what we learned is that the 80-plus population in some counties in the United States is already stranded with a population age 46 to 64 that is too small to take care of them. The leading counties in the United Statesare Palm Beach County, Sarasota County in Florida, and surprisingly, Ocean County, New Jersey, and Barnstable County on Cape Cod. Now, what those counties all have in common is they are popular retirement destinations, and the older people move to those destinations, but their families don't go with them, because there's not a job economy that matches the popularity as a retirement community. So if you think about the point that the AARP was making, and the point that we should be thinking about is, if the caregiver support ratio is projected out into the future to be inadequate to care for the population of people who are age 80-plus, what, if anything, can supplement that ? Or are people really living in the wrong areas? Are they going to have to move? What will happen? And I'm not going to offer a theory on that.

So take a look at the technology market and what's happening in that market. This is the reason we have such potential in technology to help an older population and to, in fact, help us live better in our later years—not necessarily longer, but possibly to live better. And that includes some things that have already been discussed: the miniaturization of sensors, the role of fitness wearables if they weren't in fact just about fitness. We have the ability now, for example, to have people wear inactivity monitors— monitors that say, "You haven't moved; time to get up"—and inactivity monitors on older adults. We have the ability, for example, to put sensors on people that could detect

if, in fact, you're dehydrated and you need to have a drink of water. All that kind of capability in the sensor world—sensors have become very small, very cheap. The problem is they're not integrated well, they're not applied well, and they certainly aren't tied into your electronic health records, but moving forward, that is certainly feasible.

We also have mobile broadband and GPS tracking capabilities, and you probably have heard—for a long time now, you probably heard about geofencing and the fact that it is possible to draw a circle around a geographic location and say that [if] anybody, including a dog, a cat or an older person, anybody who moves outside that circle, in fact, an alert needs to be transmitted that warns that you've moved outside that circle. That has yet to be applied effectively in the older-adult market where people have dementia. Typically they're wearing something that is not based on a geofence, and the problem with the geofence in general is somebody has to maintain it. They actually have to draw what it is, and then they have to deal with the administration of notification. So that's geofencing.

We have video and Skype everywhere. Again, [these are] not as well applied in the older-adult population, especially those who have dementia.

And we have voice activation, which I'm going to talk about a little more, because I believe that voice-activated technology is the future of useful technology for older adults. I do not believe we're going to be typing, swiping, pinching, zooming or doing things with our fingers moving forward. We are going to speak, and we possibly will speak in multiple languages, and we will be understood because the devices will have lexicons of those languages that will enable translation to occur. Voice, I think, is one of the great advances—and voice coupled with a little bit of AI that can say, one question can be phrased 17 different ways and still understood. That's the little bit of AI that's useful: vocabulary combined with the knowledge of what we care about and what we're interested in. This is really the remarkable thing.

I'm not going to get into the penalties for reimbursement or the telehealth market, I think, at this point.

So this is to me a very interesting slide. It's not generally published by Pew; they gave it to me. This is 15 years of surveys of people age 75-plus and whether they actually had access to the Internet. And what you can see is, in the year 2000, 93 percent of them did not, were not Internet users, and in the year 2015, 50 percent of them are Internet users.

Now, smartphones did not appear until 1997, and they took off between '97 and 2000, but the interesting thing about this is, while Internet usage has only progressed to the 50 percent point among the people aged 75-plus, the physical in-person resources for those people have increasingly been disappearing. You look for bank branches, post office locations; an endless number of service providers are consolidating and eliminating the physical retail location, if you will, in favor of online, and in fact, savings bonds used to be able to be bought in person. They are no longer able to be bought in person. Many of the reports out of the Social Security system are only available online now. The belief was, when the federal government went for a paperless world, they believed that the older adults who received paper information from them were online. They've retracted multiple times on these statements stopping the paper version, and there's actually a lobbying group to preserve the paper option, but the bottom line is, this is where it is for the 75-plus. So they're going to have to have a proxy or a person representing them with appropriate Internet access in order to get the resources that they need.

I'm not going to go through this study much. This will all be available in your notes, but basically the gist of it is we recently did a survey in 2015 of people age 59 to north of the age of 85 about the use of communication technologies, and what we learned is in the older population, what people wanted to be able to do was to read and send email. These are people who are online. They wanted to read and send email; they wanted to search the Internet; they wanted to be able to do Skype, view photos and particular photos and videos. They wanted to be able to see their grandchildren. And in fact, one of the interesting technology introductions that has happened in recent years is the ability to scan paper photos and store them online, because if you think about the

volume of photo albums that older adults have today—that, in fact, are going to be lost in the sands of time, because they'll just be in bundles—there are companies and services that will scan them and put them online. And they have, some of these, like this company, Keepy, a small company in California that started up to do it, discovered one of their most interested user bases was the population of older adults.

So tablet ownership declines by age. I think you'll see among the 85-plus not much interest in that. The older adults are not well represented among app downloaders. They are not particularly interested in downloading any apps. They might even have smartphones, [but] they download nothing. GPS turn-by-turn directions is something they would like to be able to do, and you and I would all like to be able to do it properly, and you'd all, I'm sure, like to have it work. That was one of the uses that they thought would be helpful, but they believed the user interface is a hassle.

In terms of smartphones and the usability of technology, I'm not going to go into that. And telehealth, not very interesting to older adults. Fitness wearables, also not that interesting to older adults. AARP, by the way, ran a test of wearables for fitness, and they gave them to a group of people all over 65, and they discovered that they struggled with the packaging, they struggled with the directions. And if any of you have ever taken a hacksaw to a clamshell package in order to get the product out of the package and then tried to understand the directions—which might not actually be in the package, they might be somewhere else, you might have to read the manual online—you can see people got frustrated in that project.

They also are not willing to pay much for telehealth technology, and they're particularly not too interested in having their children pay for it. But when it comes to some technology, they're people who wish they could use it. This guy, I really kind of love him in the study. He says, "I have two iPads, an iPhone, a laptop, two iMacs and an iWatch. They are all wonderful when they work." But the flipside of that is people are concerned that there is not enough support for the technology that they have, and that the vendors of technology are upgrading so fast that, in fact, a version that you thought was

supported and that you thought was up-to-date actually is no longer up-to-date and no longer usable. And it does appear to a lot of older-adult users that technology has been programmed and created by young people, who assume that the user will know what to do.

So in the context of the technology market, I'm going to probably zip past this, so I can get to the point about what is the market.

So these are the categories of technology for older adults that make a difference in the lives of older adults. There are four categories. They're represented in a puzzle diagram, because without one of them, the other three are not all that useful. So in the upper left, you can see that that's where all the communication technologies fit—email, chat, etc.

On the right are the security- and safety-related technologies, including the one I just mentioned, home inactivity monitoring, but also fall detection. Again, available. Lots of offerings that have fall detection. The question is whether it's being deployed properly among the older-adult population, who, in fact, is more mobile, and so the mobile personal emergency-response pendant now is 20 percent of the personal emergency-response pendant market. Five years ago, it was a very tiny percentage, but people want to be able to get out and walk the dog, and so that's why mobile capabilities came into play. Also, webcams and the ability to communicate in that regard.

On the bottom right are all the health and wellness categories, including disease management, fitness trackers, wearables, telehealth and medication management.

The bottom left, I think, is the most interesting category to help us cope with the other three, and that is the ability to learn new things, to learn online, to volunteer and to have what's now called financial wellness. And it's, in fact, a category that AARP is tracking now called fintech, which are the technologies that are available to help you manage your finances in such a way that you could actually preserve your income.

And in the middle is really the boom market, which is the market of caregiving technologies or technology-enabled caregiving, I should say, because in 205 and 2016,

$200 million worth of venture capital investment went into tech-enabled home care. Remember, I said assisted living was tough as a group environment except for dementia care. Well, home care is booming, and the VCs see an opportunity to pour money into that in the hopes of finding the perfect thing that will help this growing older-adult population and in ways that don't require 24/7 in-person presence to care for them. And those are what I call the tech-enabled home care companies, Honor, Hometeam and HomeHero, with three Care.com care links. These are all companies that are specifically focused on creating either marketplaces of caregivers or technology to deliver care and monitor that care in a way that you're monitoring the care even when the person is not in the home doing the care. So I think that's it for that.

So here are some examples of technology for seniors and their families. These have been around for a little bit. That's a medication-dispensing device on the top left called MedMinder, but the smart thing that happened in 2015 or 2016, actually, was that they became preloaded with -- from a company called Pills and Beyond. So the problem with medication dispensing in general is someone has to administer it, and that one is preloaded by the pharmacy.

There's a tablet for seniors. The target market for grandPad in the top center is actually the 85-plus age range. The personal emergency-response button that is mobile was invented by MobileHelp a few years back—they are now a $24 million company. On the right is It's Never 2 Late, which is for people with dementia, and it started out in nursing homes, and it is now an adopted technology by Brookdale in all of its dementia-care units around the U.S. Bottom left is Philips GoSafe; that's a mobile personal emergency-response capability. Sync Fit is another technology used in senior housing for people with dementia. Breezie is the tablet for seniors. Tunstall and QMedic is a mobile personal emergency-response pendant.

Those were technologies that were already out. This past year, these technologies all emerged as being useful to older adults, and as I said, I'm particularly interested in the Amazon Echo and what's happening with it now because of its interfaces. So when

Amazon shipped the Echo, a year later they created something called Amazon Echo skills, and the skills can be trained—you can use the skills technology to train for a particular purpose. One of those purposes that has been tried now is caregiving, so a custom version of speak to the Echo in terminology that's appropriate for caregiving has been introduced. And a new company has emerged called LifePod, and they're not even shipping in the market yet, and they created an application for the Amazon Echo in which you don't have to wake it up. You don't have to say, "Alexa, do something"; it wakes itself up, and it has an interaction with the person at regular intervals during the day.

There's a category of software now called cooperative care management that is in the market and a variety of other things.

On this screen, I think what's pretty clear is that on-the-wrist is becoming quite important, that caregiving-related technology like Care Angel, which is probably going to be white labeled by hospitals, is important. Care Angel is an interesting technology. What the hospital might do with Care Angel, they might have the hospital-specific version of it that calls the person automatically through the system and says, "Mom, this is your son," or "Mom, this is the discharge planner," [or] "This is your son through the discharge planner for the hospital, and this is a reminder that you need to take your medications." I think, as applied by discharge planner or a nurse that the older person is familiar with, this is IVR—it's interactive voice-response capability. Press 2 if you're okay, press 3 if you're not so okay, and press 1 if you're in dire need. You may find that rather startling, but that actually is—. There are at least three companies that entered in the past year that are in the space of interactive voice-response technology, and the reason for that, of course, is to minimize the amount of resources required to follow up on an older person after they have, in fact, left the hospital or if they're in a relatively frail state.

In the middle is an important capability that is not yet applied widely to older adults, and that's the Piper proximity beacon. What a proximity beacon is, it's a device placed in your pocket, and as you move with that device, the device can interact with a system and customize the interaction with you based on what it knows about you. So

you're wearing this device, you have dementia, you walk up to a computer, we'll say, in a dementia unit, and all of a sudden your music starts playing, your videos start running, images that you're familiar with, and they're all activated by a tiny beacon that's in your pocket. And that's what this thing is.

So this is where we're headed in the future is all of these individual segments actually are aware of the other segments that are on this picture, whether it's home hubs or home automation, durable medical equipment. They are looking for new lines of offerings to deliver to older adults. Home remodeling, home builders' associations, certified aging and place specialists—all kinds of capabilities are out there trying to figure out a way to cross-sell and include the other capabilities so they can (a) enhance their own revenue streams and (b) provide a broader range of services that could be useful to older adults and their families who might have the money to pay for them.

So this is the way I see the future moving in the technology market. We've had a lot of technologies that were invented specifically for the older-adult population, and what I think is going to happen is those are going to go away, and what they'll be replaced with is a software-driven world that will take the technologies that every one of us uses in our daily lives and, using software, apply it to an older adult population. That is the future of technology for older adults, because [in] the other future, the one in which technologies were specifically created, little by little the market is too niche, too small to make really viable companies. And so it includes all of that on the right, which robots in car technology, all kinds of good stuff and software can customize all of it for the specific purpose of helping an older adult. And I just described to you what was happening with the Amazon Echo. That is only one small example.

That's my contact information, and I'll be available for questions at the end. Thank   you.

ALLEN KLEIN: Thank you, Laurie. Our third speaker is going to be Dr. Phil Smalley. Dr. Smalley is a senior vice president and global chief medical officer of RGA International Corporation. He is responsible for medical research and for assisting in

product development. Dr. Smalley is an internal-medicine specialist with 24 years of experience in insurance medicine. His medical degree is from the University of Toronto, and he is a past president of the Canadian Life Insurance Medical Officers Association. Dr. Smalley is also managing director of the Longer Life Foundation, which funds mortality research at Washington University in St. Louis. I also serve on the Longer Life Foundation Advisory Board and have been working with Phil for a number of years on that. The mission of the Longer Life Foundation—which is not on Phil's résumé, but I thought you would be interested in it—is to find ways for certain select segments of the population to live longer.

So please welcome Phil.

DR. PHILIP SMALLEY: Thank you very much, Al. Thank all of you. This topic of precision medicine is something I've been giving talks on a bit around the world and within North America as well, and obviously there's a lot of medical advances and even in this room, with medical colleagues in the back, Dr. Tim Meagher and Marc-André Belzil, with whom I've worked, and also probably with others in this room. You're probably talking with your doctors at your various companies about some of the medical drivers and the other points that Al has talked about that are driving, not just overall mortality, but also longevity in the older ages. We will have time at the end here with the question-and-answer period, and then I'm presenting again on another panel on Friday, giving a vignette about what medical care in 2050 is going to look like.

So I think there are some interesting kinds of advances in cardiology, advances in infections, and advances in Alzheimer's disease; definitely we can talk about them in the question-and-answer period, but as I said, I was asked today really to give an overview in the next 30 minutes more of precision medicine. This is really underscoring the importance of genetics that Al has already touched on. The definition of precision medicine does vary in the literature. Millions of dollars are being put into precision medicine in America and other countries. It is mostly aimed at, like, a cancer and finding various targets—genetics targets or the products that the genes make as targets—and

finding a perfect medication that just attacks that target. That's one of the concepts of precision medicine. But also, this term is generalized more toward the concept of individualized care, personalized medicine, and I'm going to be talking a little bit about both of these, really showing the importance of looking at the person's genetics or looking at the person who has cancer, looking at the cancer cell genetics to be able to better treat the patient. So we're looking at genes, and together with lifestyle factors, environmental factors, to either be able to more accurately stratify a patient or, more preferably, to be able to better treat the patient by giving the right drug, at the right dose, at the right time.

So I think, as Al has talked about, you've seen this in the lay press when it was published, and it's mentioned that doctors are the number-three cause of death in North America. Obviously, it's not that we doctors make mistakes. What you can see here in these statistics is that a lot of this cause of mortality is due to drug side effects. When somebody is admitted to the hospital with a medical condition, 17 percent of these patients develop some serious adverse drug reaction.

It is so important that we look at these genetic risk factors and try to be able to prevent these side effects. I think society in the next few years is going to look back at the way we practice medicine right now and think we're archaic, we're barbaric the way we treat patients. I mean if the three of you, let's just say, here in the front came to see me with a medical condition like diabetes or hypertension, I would take your history, and I would say, "Well, you're all fairly similar to the group of people here, [so] I'm going to treat you all with the same drug to treat that medical condition."

Well, you, sir, no problem at all; the pill worked fantastic. It treated your hypertension or whatever; you can go away. And the other gentleman beside, unfortunately, the pill didn't really work well, but we were able to change it to a pill that worked extremely well. You here in the front, sir, I'm very sorry: You died of a side effect of the medication.

You look at this as the way we treat patients and realize we can be much more

accurate by looking at the person's genetics, and/or the cancer cell's genetics, in light of the environment and lifestyle factors to try to avoid this important cause of morbidity and mortality.

Just in this room, how many people have had some form of a genetic test? Has anybody spit in the jar or seen your doctor because of a bad family history? A handful of people or so in this room. There was a survey that was done that about 6 percent of the population has had some form of genetic test, and about 81 percent of those people felt that that information was valuable. Well, one thing that you have to consider, though, is the downside of this whole idea of pharmacogenomics is the time it takes to get the test result, as well as the cost of getting genetic information before prescribing a certain drug. So I could just say that if I had my entire genome on my smartphone in my back pocket, and then you come into my office and I'm about to write the prescription, and I give you that medication, and you say, "Oh, wait a second, Doctor, does this information about my genome actually change your decision?" I'm going to say, "Oh, wow, yes, it will." I'll either give a different dose or use a different medication.

So this is something that we're going to be seeing much more in the future with a decrease in the cost of genetic testing, maybe even genetic testing from birth. But again, what is the implication of this and the privacy concerns and the potential risk of anti-selection and other things, the problems we might have in insurance, etc.? Obviously, this is something we're going to have to deal with going forward, because I do think we're going to see a lot more routine use of genetic testing to be able to treat people with different diseases and better risk stratify and prevent various impairments.

So this is an important and growing field, this whole drug-gene interaction. Seven percent of all of the drugs that were ever approved by the FDA [U.S. Food and Drug Administration] have got some drug-gene interaction. There's a website you can go to, listing medications that have drug-gene interactions; they're labeled by colors on how important that drug-gene interaction is to clinical care. In 2015, close to 30 percent of the drugs approved have a drug-gene interaction, and these drugs and the genes—the drugs

I'm going to be talking about—it really spans many of the common diseases that we see in public health, like examples here on the chart: We can see medications around anti-inflammatories, we can see pain medicines, psychiatric drugs, blood thinners, medications used to treat infections, even some of your anti-cholesterol drugs. [For] all of these, if you knew your genetic profile, we might use a different dose of the drug or use a different class of drugs. So this is already being used in clinical care to some degree, but this is just going to expand into the future.

So I think you can see that this is something that is going to be extremely important. So let me go through about four or so examples of pharmacogenomics being used—either it's mandated or where it could be used if that information were accessible.

Abacavir is one drug. It's used to treat HIV infection, and there's 5 to 8 percent of the population, when they're exposed to this medication, get a life-threatening allergic-type reaction. Well, we can look at somebody's genetic trait that's coding for a particular HLA, an immune type that you're carrying around with you, and if you've got this particular genetic trait that I've mentioned here on the slide, these people have got a very high risk of developing this life-threatening allergic reaction. The importance of this is so key that the FDA has labeled this drug that doctors must screen the person for this genetic trait before starting this medication.

The same has been used in Hong Kong for an anti-seizure drug called carbamazepine, saying that there must be genetic analysis done before prescribing this drug to avoid life-threatening allergic reactions.

Now let's turn to a cancer therapy that we use, and one of the complications that can occur with this class of drugs called anthracyclines, used to treat many different forms of cancer as a form of chemotherapy, is that it does not just kill the cancer cells, it can kill the heart muscle. Now, maybe up to 50 percent of patients treated with this class of drugs for their cancer will get some cardiac toxicity, but 5 to 16 percent will get bad heart failure. I think you know that cancer is a bad disease, but congestive heart failure has a five-year mortality that's probably similar to some of the worst forms of cancer. So,

again, you might treat the patient's cancer, but then you leave them with a bad complication that has a worse mortality than the cancer. So can we be more scientific on which patients to give this form of chemotherapy to or what dose to use? This is what's so exciting, because we do know that there are certain genes that you might have that increase your risk of toxicity, but also there are some genes that protect you from the toxicity to this class of medications.

So I've given a presentation fairly recently with a pharmacogenomics expert from British Columbia in Canada, and he actually offers a service to allow oncologists to get the patient's genome testing done. He's developed an index to help the cancer doctor to be able to say what is actually this person's risk for developing this particular side effect, and then they can talk to the patient with informed information, genetics and clinical, to say, "What dose of the medication should we use?" We can be a lot more precise with treating cancer patients. So this is something that you can see we're going to be using a lot more into the future, and this is, as I said, not, just thinking about the future; this is already being used in some forms of clinical practice.

Now, turning to some prodrugs and the way genes metabolize medications. This is extremely important for a number of classes of medications. I'm going to start with one that you probably well know; it's codeine. Tylenol #2, Tylenol #3—they've got codeine in it. Well, a lot of medications that you take by mouth, the medication you take is not active or very minimally so. Codeine is an example. What has to happen is you take the codeine into your mouth, the pain medicine, and your body will metabolize that codeine to the active form of the medication, which is actually morphine. So if you've got a genetic variant which means that you are a super-metabolizer, where these people convert all of that codeine over to morphine, they can get very sick at even a standard dose and develop such serious side effects from taking a standard dose of codeine. There was a tragedy that happened a few years ago of a teenager who had a tonsillectomy and was given a standard dose of codeine to treat the pain and died of a complication of morphine overdose. This person was one of the 1 to 2 percent of the population who are ultra-rapid

metabolizers because of their specific genes they've got, [which] means that they just turn all that codeine into morphine extremely quickly.

And the opposite is also true. We've seen people at claims time and during underwriting who are on enough codeine that could kill a horse. They're on tons of it, and we think, "Why are they needing so much of this narcotic?" Well, these people have got a genetic deck of cards such that they don't make those proteins to metabolize the codeine to morphine, so they need extremely high doses. Again, if we knew that you were one of that 5 to 10 percent with chronic pain on disability claim and we could then say, "Well, codeine is not the right pain medicine for you. Change it to a different class of pain medicine," we could then decrease some of their disability risk, possibly get them back to work and potentially prevent some complications that could occur.

And this is not just with codeine. The story of prodrugs extends to other drugs. There is the antiplatelet medication Plavix, that goes through the same process. Tamoxifen is also very interesting. It is used in breast cancer patients. After the breast cancer has been removed surgically, a lot of women who have hormone-receptor-positive breast cancer are treated afterward for five to 10 years with this medication. Well, again, it's a promedication: If you take the pill, it has to be metabolized into an active form to be able to prevent the breast cancer from coming back again.

Well, again, some women are born with a genetic mutation where they cannot convert the tamoxifen to the active ingredient. So doesn't it just make sense, then, to test the woman in advance of whether or not you've got the genetic mutation to know should we use that medication or a different class of anti-cancer therapy to try to prevent the cancer from coming back? For insurance purposes, when we underwrite a woman with breast cancer and she's on tamoxifen, we know [in] the people that are responding well to the tamoxifen, the chance of their cancer coming back would be less. So it just seems to me to be almost a no-brainer that we should be looking at a patient's genetic profile in combination with lifestyle and their environment to be able to better assess them and better be able to treat them going forward.

Warfarin is another good example of pharmacogenomics that could be used, and it's already being used in practice in some centers. Warfarin is actually rat poison; I think you might know this. The way warfarin kills a rat is it's a blood thinner. When the rat eats this warfarin, it causes bleeding into the brain, stroke, bleeding into the gut, and it kills the rat. Well, we use this blood thinner in patients who come to the emergency room with blood clots or their heart is not beating regularly and they've got atrial fibrillation. Well, using this drug also has important implications in a human, as this drug can cause strokes or death. When someone with a blood clot or atrial fibrillation comes to the hospital and they're put on the warfarin, we try to give them the right dose; we follow them carefully. Unfortunately, some people's blood gets too thin on the warfarin, and they have a risk of having a major bleed, especially in the first year. But, if we don't give them enough of the blood thinner, the blood clot that is down their leg could get worse, break off, and kill them with a blood clot going up to the lung or that can cause a stroke because their blood is not thin enough with the warfarin.

Sometimes trying to get right dose of this warfarin is extremely difficult. Again, as I mentioned with my example before, the way we now treat a patient is we look at their clinical parameters and other things that they might have, but we commonly give all the starting dose of the warfarin, and then we would say, "Come back in a few days or weeks. Keep following your blood and see how thin it is." We then might see that the dose of warfarin was too high for you—your blood is a bit too thin, you'd better hold the pill, or we give you a medication to reverse it—or we didn't give you enough at the start.

Well, now you can go to a website that was developed—again, it was a study that we funded through the Longer Life Foundation with Dr. Gage—and the doctor can enter in the clinical information on the patient but also look at their genetic profile to see how sensitive you are to warfarin. And you can now tell the doctor immediately, based on all this information along with the genetic information, that you should start at the lower dose of the warfarin right off the start. And this can be successful. There was a meta-analysis done out of 11 trials that showed that by using this kind of genetic information

along with the clinical information to dose a patient, we can decrease this major bleeding complication by 64 percent, and we're getting the right level of blood thinning to be able to reduce the significant adverse events by 14 percent.

But you kind of wonder, and it seems so obvious that we should therefore be looking at people's genetics, but the FDA and other regulatory or pharmaceutical societies, associations around the world, for many of the drugs I'm talking about here other than abacavir, the associations say you don't have to know the genetic information. You just start at a low dose, you follow the patient, and you slowly increase it, and it takes time to get that medication to the right dose. Unfortunately, it takes time to get that genetic test done to be able to better treat the patient, and there's a cost to getting that genetic information test done.

I still think there's an argument to say if I already had my genome in my back pocket, that whole problem falls away. I would much rather let the doctors use all of their abilities along with my genetic information to properly dose me and choose the right medication. So there are some insurance products around the world that are looking at using this kind of technology as a wellness benefit when somebody buys insurance products, so they've got this in their back pocket to be able to help, should they ever need some of these medications in the future.

These drug side effects are so important, and I think we can really limit this cause of morbidity and mortality going forward.

Now, the other portion of precision medicine that I've talked to you about already or introduced is the concept of targeted therapies, and the poster child for this is a form of leukemia. It's chronic myeloid myelogenous leukemia. It's a terrible form of leukemia, and in the past, you're probably looking at needing a bone marrow transplant or dying within five years of having this form of leukemia. Well, because we knew the genetic abnormality that caused the leukemia, we were then able to find one medication that just blocked that gene product, and just the cancer cells die away. It does nothing to all the other normal cells. This is really exciting, and it has really changed the treatment of

chronic myelogenous leukemia. You've now got a five-year survival of about 96.2 percent. So this has been something: [With] a disease that we would have been very concerned about in the past, now people can just take a pill a day, and they can be living quite a good quality and quantity of life.

The problem with a lot of forms of cancer and a question that is commonly asked by our actuaries is, Are we going to, over the next few decades, completely eliminate cancer morality with all these new technologies? And one of the problems and [reasons] why we're fairly pessimistic of completely eliminating cancer mortality—although I think we're going to improve cancer mortality— is that cancer is not just one disease. It's obviously multiple different diseases itself, different genetic etiologies, and even within the cancer itself, it's not just one cell that's growing. There are other cells that might be growing, so you might kill off one group, but the other portions of the cancer that have a different genetic mutation could continue growing, or the cells get resistant to these new forms of targeted therapy, so then we have second-line therapies that then can be used. But a common theme I'm going to be telling you over the next few slides is to look at the cost per year that these people are going to incur, as they have to be on one of these medicines for the long term, and when we start thinking about some of the reimbursement of health care products, this could be an issue.

So you see, we knew the gene, we knew the abnormal protein that was made. We then use precision medicine to just attack that protein. And this is a common theme that we're seeing in many different forms of cancer, and a lot of research is going down this way to be able to improve the case fatality rate with cancer going forward.

Targeted immunotherapy. Again, Al Klein talked a bit about this already, but again, it's looking at the genetics, not of the person, but of the cancer cell itself. Looking at people with very bad forms of skin cancer, melanoma that's quite advanced, 60 percent of these patients do have a particular genetic mutation, and if you've got this specific genetic mutation when you analyze the cancer, these people respond quite well to this form of targeted therapy, and it does improve survival. You can see with standard

chemotherapy, you're living with this form of advanced melanoma for about 10 months, and we can extend life expectancy in these patients now up to about 14 months and then, using multiple forms of these medications, maybe even a lot longer still. But then you would have to ask yourself the question, Well, for what looks like a fairly minimal increase in life expectancy, even though it's statistically significant, is it worth this cost, and how much more improvement are we going to be able to achieve in the future to completely eliminate stage 4 cancer mortality? And that's one of the things I've put in my vignette for Friday.

Now, there are different BRAF mutations as well in these forms of melanoma, and if you've got kind of a wild type, again, by looking at the genetics of the cancer cell, there's another new class of medications called checkpoint inhibitors that can be used. Again, another form of precision medicine: By looking at the genetics of the cancer cell again, we can improve survival by about 58 percent in patients with bad, advanced forms of melanoma and other forms of cancer as well.

There is even one study that came out looking at women with breast cancer. I've already mentioned that they are commonly put on tamoxifen, but also in some women with breast cancer, the clinical features of the cancer, such as where it might have spread or the size of the cancer, might mean that the patient needs chemotherapy after the breast cancer has been removed. Well, these people, when we look at the genetics of the breast cancer cells, the study showed that there are some women that the genetics of the cancer cell actually look like it's a low risk, and maybe we don't need to treat those women with this form of cytotoxic, bad chemotherapy. And maybe up to 40 percent of women maybe didn't need chemotherapy that could cause a lot of side effects. Again, this is the way of tailoring therapy by looking at the genetics of the cancer cell itself.

And it is not just cancer that is using precision medicine. A juvenile disease called cystic fibrosis—it's a big umbrella term for multiple different types of cystic fibrosis. There are different genetic types that cause a different change in this chloride receptor, therefore causing cystic fibrosis. You can have different genetic mutations causing

different abnormalities in the receptor. And now, by using precision medicine, when we look at the patient's genetics, we can then say, well, some people have got a particular mutation that they respond very well to a form of targeted therapy, improving some of the complications, such as the lung complications and the gastrointestinal complications associated with cystic fibrosis. But then again, my general theme: These are children who would need years of these new medicines, and look at the cost of this medication per year. Will society be able to afford this? Sometimes we're making very difficult decisions with limited health care dollars, to be able to extend somebody's life expectancy with cancer or cystic fibrosis.

Now looking at diabetes, the most common forms of diabetes are multifactorial, multi-gene-types disease. But 2 percent of diabetics have a monogenetic form, so there's one specific mutation that causes that patient's diabetes. Now, as I said, it's not that common; it's usually in the less-than-25-year-olds, this maturity-onset diabetes of youth. They look like the adult form, but it occurs at the younger ages, and again, looking at the person's genetics can help us to tailor therapy. So we found that [in] some people who have got one specific mutation in this group of people, their diabetes is extremely mild. We might not have to treat it at all. It doesn't seem that they develop the diabetes complications, even though the doctors label them as having diabetes.

Well, another group of people with the form of maturity-onset diabetes in youth, these people have a different specific genetic cause to the diabetes. That means that they respond very well to a different class of diabetes drugs, compared to what you were hearing about from Dr. Barzilai earlier this morning. They respond very well to sulfonylureas. So you see the concept here that, instead of just putting all patients into a big bucket and treating them all the same, by looking at the diabetics' genetics, we can better stratify their risks, we can better treat them with the right drug and at the right dose—even looking at exercise to treat these people. There are some genes that say you might be carrying genetic traits that mean you might respond better to high-intensity exercises. Or maybe you might respond more to resistance training. You might be more

of a sprinter type, or you might respond more to aerobic-type exercise. Even dietary management might alter if you're carrying one of the Alzheimer's genes, an ApoE4. Maybe you respond to a different type of diet more favorably compared to general diet recommendations that are given to the whole public to follow.

So you see my general theme where we're going? I'm looking at the positives of genetic information to be able to help us to better treat patients.

One of the medications that have now been approved is a drug that is more than a million euros. This is not a precision medicine that is targeting the gene product; this is now looking along the lines of what Al talked about with altering the abnormal gene itself or giving the patient back the gene that they're missing. It's a very rare disease, about one in a million people, but some people are born with a mutated gene where they cannot break down fats that are in their blood. Their blood actually looks like a pink sauce, it's so full of lipids and different formed triglycerides and cholesterol, because they're missing this gene to break these lipids down.

So what we've now got is a form of gene therapy where we can give you a vector that carries that normal gene, and now that works for a while in the body, and all those fats get metabolized, and all those bad complications that these people have with this genetic abnormality go away. But unfortunately, those cells start dying off that were infected with that gene therapy, and then you have to give it again. But again, look at its cost. This is a form of therapy that has been approved in Europe, not in North America, but you see this idea.

So I've talked about using genetics to be able to avoid some drug side effects. I've talked about using your genetics to be able to target therapy in various diseases, and we can potentially change the genome itself, but many of these therapies, like Al talked about, have the potential of side effects. When we start interfering with the DNA, it's already shown in some studies that we can cause cancers. And actually, Al brought up the CRISPR techniques, and some of these, you take the cells of the cancer out, and we put them in a petri dish, and we try to charge up their white cells to fight the cancer, and then

we put them back into the cancer patient. It works extremely well, but one of the reasons why we know it's working so well is the patient gets really sick. They need to be in the intensive-care unit because their white cells are attacking the cancer so aggressively, and again, that can cause morbidity and mortality. So we're learning a lot with this line of research. We're designing and finding new drugs to be able to treat diseases.

So overall, what I really want the message you take away from this [to be] is I think you well know that one size does not fit all. This is the concept of precision medicine—individualized care, personalized medicine. Precision medicine is already being used. This is not just future thinking. It's going to expand quite a bit into the future, and all of this should improve disease outcomes and decrease drug side effects, all which I think are going to improve public health and help us in the insurance industry. Thank you all very much.

ALLEN KLEIN: Thank you, Phil. We have time for questions now. Please come to the microphone, state your name and affiliation, and ask your question to any of us.

S. JAY OLSHANSKY: Jay Olshansky, University of Illinois. Really, a brilliant set of presentations. I really enjoyed this, by the way. I have questions for all of you, but I'm going to start with Al, since you're standing at the microphone.

So you had a really comprehensive list of variables to look at, and what I'm anticipating from you—correct me if I'm wrong—is that you are going to come up with a new schedule of age-specific death rates in the future, based on where you think all of these advances or changes or factors are going to going to play out in the future. Is that where you are headed with this, and if so, how do you go from each of those drivers to an estimated change in mortality? I'm just wondering how you and your team are going to do that.

ALLEN KLEIN: It is a great question, but we are not going to do that. We are going to put together some thoughts on quantifying the drivers, but quantifying them is beyond our initial scope for this project. One of the things that I did not mention that we are going to do is to take a look at the drivers from the perspective of both developed

countries and developing countries. We think they are going to be different, so we are going to look at that, but we are not going to try to quantify the drivers, as this goes beyond what we are able to do, at least at this time—maybe in the future.

S. JAY OLSHANSKY: I also have another question for you. If you were, let's say, in a developing country and you were thinking of what could I practically do if you were just an ordinary person, out of all these drivers of mortality, is there something that is within people's control? What are one or two or three things that are really in their control that you think they might be able to influence with these drivers?

ALLEN KLEIN: The first one that comes right to mind is stick with the diet that you have, because the developing countries typically eat naturally. They don't consume all the processed foods which are causing problems in the developed countries. I have read some articles about native populations that are all healthy until they bring in the McDonald's. Then these populations begin to get unhealthy; they get the same heart disease that we have. They are actually very healthy by sticking with the diets that they currently eat. They may not live quite as long, partly because some of them are still hunters and get hunted themselves.

They also don't have the stress that we do in the everyday world. They have different stresses, but it is not quite the same.

They spend much of their time outdoors, and that is healthy and should be continued. I just read something within the last day or two that the reason so many of us are wearing glasses and have bad eyesight is because we do not spend enough time outside as we are young and as we are growing up. So those that are in more of the developing countries do spend more time outside, and you will find that they do not have as many vision problems as we do.

So those are few thoughts.

S. JAY OLSHANSKY: What about developed?

ALLEN KLEIN: Developed countries—I believe stress is one of the biggest killers. We need to be able to better control it. I have tried meditation myself but have had some

trouble doing it. For some, like me, it is very difficult to do, but there are many ways to do it and other things that help out as well. I think some people are good with coping with stress, while others are not, and stress is an important factor. Diet, again, is also important. Sometimes what you read about is not the right thing, which is why I just touched on this. Another thing that is important that I did not mention before is getting enough sleep.

Exercise is important, but from a resistance standpoint as well as a cardio standpoint. Also, as I mentioned before, just getting up and moving is important. We sit at our desk all day long, which is not a good thing, so that is another factor for developed countries. In summary, it is the things you probably know—diet and exercise—but it is doing it the right way.

PHILIP SMALLEY: Can I say one point?

ALLEN KLEIN: Please.

PHILIP SMALLEY: Yeah, just, there's one thing that I think is starting to become very clear, [which] is that everything fails. Nothing works on its own, and I think if we really are going to make a change to public health, especially if we start looking at lifestyle, it's got to be a more multifaceted type [of] program.

All diets fail. Telling somebody about their genetic risk or telling them about stopping smoking, each one element, telling them to exercise—people will be able to do it usually for six months to a year, then they fall off the wagon. If we're going to really make a change, I think we've got to find an affordable way to try to encourage the use of psychology and coupling that with a trainer, coupling that with food that is affordable and delivered in such a way—using a whole program together with the human touch. This is why I was very interested in the use of the technology.

I think just giving somebody a wearable and it's not connected to a human without any ongoing coaching—this is something that's just destined to fail. And I think using a program that is all together is something we've got to start looking at more.

ALLEN KLEIN: Phil made me think of one other thing, and that is the reason diets do

not typically work is because people do them for a short period of time and then stop. This needs to be a lifetime commitment to change. Using some of the new technology also helps. How many of you use Fitbits or something like that? It is kind of challenging. You want to get those steps in each day, so that's a good thing. It really is! Scott.

SCOTT RUSHING: Sure. My name is Scott Rushing, and I work with Phil at RGA. My question is for Phil. You're sort of encouraging people to get their genetic profiles, so let's say you go online and order your profile (or go to a lab or whatever). The concept of precision medicine is that you can use the genetic profile along with traditional medicine to be a little more effective. What if you were to walk into your doctor with your genetic mapping on your phone or 100-page printout or however it comes out. Is a typical doctor going to even know what to do with the information or what they're looking at? My second question is, I notice only Phil's presentation online. Are the other two coming?

ALLEN KLEIN: Yes, the other two presentations will be available online.

PHILIP SMALLEY: And the first question is commonly asked when I give talks on genetics, and I must say I'm probably a little bit on the bullish side compared to some of my other insurance medical colleagues in this area. I do think there are a lot of advantages, and a lot of my colleagues would debate this. They're concerned that we're just arming the population with information that legally we might not be able to look at anyway—the anti-selection risk. And a big thing that is always asked is, are we too far ahead of the clinical curve?

And I think that's what you're getting at, Scott, because when we've talked to various clinicians about using genetic testing of the cancer cell, well, in some forms of cancer, it has to be done anyway, but it's usually just a certain panel. Or there's a lot of interest in getting all of the genetic information to help both the patient and potentially their family, but as you're alluding to, the clinical doctors have not yet been trained and know how to use this genetic information. And I think it's going to take the use of technology like that website where you can put in the genetic information and out spits an answer to help the doctor to be able to use this complicated form of information. And,

remember, it's not just one time. You get your genes, where medical research continues, so maybe you're going to tell the patient they might have low risk, but later new research shows new mutations and alters this assessment There's one study that showed that those people that are in-between heart attack risk and you're not sure if you should put them on a statin or not, [for] 12 percent of those people, the doctor would change their decision and put them into a high-risk category if you just looked at their genetic cardiovascular score. So maybe you might tell your patient that their genetic profile looks like they are at a low risk, so let's wait to start the cholesterol drug. A year down the road, a new study might come out, and [you] say, "Hey, there's a new gene that we didn't know about in the past, but we've now got a new study to show that it is really important. I now think we should start you on the therapy."

So I think that it's going to take a while for the clinical world to catch up to be able to use this genetic information appropriately, but it is already being used.

ALLEN KLEIN: Phil, just a quick corollary to that. So when do you think it will be before the doctors are able to use this information, or at least the vast majority of them?

PHILIP SMALLEY: As I said, it's already being done in some scenarios, but not looking at your entire genome, the whole genome sequencing. It gets so complicating; there are so many gene abnormalities that we find that we don't know whether they're significant or not. I found it fascinating to get my genome looked at, and I knew that there were some things I found about myself that I didn't know I was at risk on. It was a family problem actually, because I didn't know whether or not I needed to talk to my family about it.

TIM MEAGHER: Tim Meagher, Munich Re, Montreal. I'm just intrigued by your selection of the 11 variants that you're going to look at. You mentioned you had some sort of democratic process. You got it from 18 down to 11. Could you just tell us about the seven that struck out and didn't make it to the list?

ALLEN KLEIN: None were actually struck. They were combined into broader categories. We were also trying to cull it down to a more reasonable size. One example is

that we initially had smoking and exercise/physical activity as separate drivers; we combined these into the broader lifestyle category you saw in the presentation.

Jay and Scott, also to answer your questions, this session was a late add. If anyone signed up for the symposium right when it was open for registration, this session was still not even thought of. This is primarily why our presentations were not all available, but they will be when the revised presentations are posted.

S. JAY OLSHANSKY: So I have a bit of a hypothetical for anyone up there who wishes to answer. So paint a picture for me, and Phil, I know you may be doing this on Friday, but if you could paint a picture of the future, in this perfect world where we have personalized medicine and we're able to sequence the genome of the particular cancer that's influenced us, and we positively influenced that whole list of variables in a way that we maximize health and longevity, and you're in this perfect hypothetical world, how much longer do we live relative to today?

PHILLIP SMALLEY: You want to bet for a lot of money for a 150-year life span? It's a very good question, of course, and trying to look in a crystal ball on how far we can extend life with all of the new forms of therapy that could be given to alter lifestyle and do precision medicine, I really think it's going to continue to be a positive force. But how many more years? I think there was some work done in the U.K. using death by cause and copula functions, looking at just eliminating one cause of death or cancer, and that increases life expectancy by about 3.3 years. And if the disease is very interdependent with other diseases, it might increase life expectancy by eight years.

But if you're talking about moving the needle on life span, how far can you actually ultimately live? How many beats of the heart does the human being actually have? I would be siding more on your point of view, The oldest woman now is an Italian woman who is 117, so it's going to be five years at least to see if she can live longer than Jeanne Calment's 122-year life span, and then going forward after this, I think it's going to be really hard to push that life span. But I do think we're going to see significantly more squaring off of the survival curve. Is that fair to say?

ALLEN KLEIN: I think life expectancy will continue to increase, but I do not know to what. I believe there will be limits, because we cannot get to an ideal world, as there is too much money to be made when we do not have an ideal world. To get to an ideal world, we would need to push out life span, which we can only do if something like the parabiosis that I mentioned comes to fruition and really does work—that is, that blood transfusions help to keep one young for at least some extended time. It may be possible to push our life span out, but right now, there is nothing that does that.

So I see life expectancy increasing, but maybe not to the extent others do. People could certainly live longer healthier, which I know is one of your key issues. This would be done by eliminating some of the diseases through treatments and other advances, but I don't know exactly how much further we can live without an increase in life span itself.

LAURIE ORLOV: I do want to add, if you have not seen the *New York Times* article about the 98-year-old woman who was doing ballroom dancing and yoga, just search for *New York Times*, ballroom dancing and yoga. She's dancing up a storm, and the picture of her in the *New York Times* in a yoga position is quite impressive.

MICHAEL BANKER: I guess, going back to the personalized genetic mapping, you mentioned anti-selection in a word. There are a lot of discussions about the terms around that, but listening to you guys, I'm wondering, maybe there's a mitigating aspect to the fact that if you get genetic testing, there are benefits to it potentially. Do you have any thoughts—obviously from a life insurance perspective rather than annuities or health— whether or not anti-selection really should be an issue or whether maybe it's not such a big concern for us?

PHILIP SMALLEY: Of course, it's something that we're wrestling with the law in many countries. Right now, it's a very hot topic in Canada about whether or not we can use genetic information at all or genetic traits at all for underwriting, and it's something that we're wrestling with around the world. No country that I know of around the world, when somebody applies for insurance, will order a genetic test. But again, knowing some of these genetics and being able to use their information when they've already developed

a disease, to be able to help better risk stratify—it's just another medical advance that should allow us to insure more people at better rates, and I think genetic testing is going to get ubiquitous anyway. As I said, I think we're all going to be getting some form of genetic testing done, in the near future, maybe even from birth.

But realize that it's not just your genes. Somebody could, like Angelina Jolie, for example, be carrying the abnormal BRCA gene, but she also has a bad family history. A lot of the studies that look at what's called penetrance, the risk that you'll develop the disease because you've got the genetic abnormality, realize—like my example with the cancer chemotherapy and cardiac toxicity—there are genes that, yes, increase your risk, but there are also genes that decrease your risk. So you can't just look at your genetic profile out in isolation without being in context to the other information like your family history, and we need more research to be able to analyze that. Even telling somebody who has a poor lifestyle that they have a really high risk of a particular disease—it does not change behavior in the long term. It has to be coupled with other forms of technology and other forms of lifestyle behavior modification techniques.

MICHAEL BANKER: Sure. I guess what I'm really thinking about, though, is, like you said, we can't use this right now, so you have people who are going out and getting it. And increasingly, as the costs come down, this will happen more. So assuming that regulatorily, we still can't use it, then you have this asymmetric information.

PHILIP SMALLEY: Exactly right.

MICHAEL BANKER: They know they're at risk, and we don't know.

PHILIP SMALLEY: That's so true, and it depends on the country, and here in the States, you've got GINA [the Genetic Information Nondiscrimination Act of 2008] that's restricting the use of underwriting genetic information for some insurance products. It hasn't yet impacted some of our life insurance products, but definitely that anti-selection potential is there. But it was funny, one of the things is I found out from my genetic assessment is I am carrying one of the Alzheimer's genes. Well, everybody here in the room has about an 11 percent chance of developing Alzheimer's disease. Because I've

got one ApoE4 allele, I've got a double risk, 22 percent risk. Well, when I talk to the underwriters in various companies and ask what they would do with me carrying that gene, "Even if you can use that information in some country," they said, "we have a bit of concern of you applying for long-term care or something else." And I said, "All right, I understand that you might be concerned about this one factor, but what about all these genes that I don't have? I don't have BRCA, I don't have any genes for Parkinson's disease. If you're going to debit me for my one, why not credit me for these other positive things?"

So I think we're going to see so many people knowing their genetics, of course. Could this impact pricing and how we look at insurance products in the future? I also see the benefits of genetics and not just the concern of anti-selection. But there's been a lot of research that's been done in Canada. Myself and other physicians in insurance medicine in Canada have worked with some actuaries to look at what the potential impact could be on pricing, and this is a project that's being repeated in the United States to see how much really would be the impact if we, up to a certain amount of sum assured, allowed people to anti-select against us and we could do nothing about it. So I think the story is still out.

All I can tell you [is] in the U.K., they've had a moratorium in place for quite a few years where the underwriters had to ignore any genetic information, even if it was declared, and it really has not resulted in a significant impact as of yet. But with more genetic testing available, more living-benefits products, it's something we're going to have to continue to follow with more research.

ALLEN KLEIN: Okay, we are out of time, but I have one quick question for Laurie, just to finish up. So you mentioned a bunch of new technologies and upcoming technologies. Can you pick one that is going to have the biggest impact, in your opinion, on our lives in the future?

LAURIE ORLOV: Well, a mobile, wearable technology that would help us prevent falls. I think we're going to have a combination of a mobile wearable technology, and

we're going to have an in-home technology like I described, like the Amazon Echo, and both of those will be addressed by voice. There already are products now [where] you can speak to devices. We're not going to be typing; we're not going to be pressing buttons; we're not going to be feeling around a too-small Apple watch. We're going to have the ability to speak, hopefully in a private place.

ALLEN KLEIN: Thank you. And thank you for all your participation. Hopefully, you learned how to live longer as well as learning something professionally, too.