Cost-Effectiveness Determinants and Data Needs
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DR. McCABE: Now, Dr. David Veenstra will discuss cost-effectiveness analyses of genetic technologies and informed coverage and reimbursement decisions and the data needed for conducting such analyses. Dr. Veenstra recently joined the University of California-San Francisco School of Pharmacy and is an assistant professor in the Department of Clinical Pharmacy.

Dr. Veenstra?

DR. VEENSTRA: Thanks to the committee for inviting me to come and present today.

The other speakers I think really gave a great background for talking about cost-effectiveness. I just want to give a little bit of an overview of cost-effectiveness, kind of the 20,000-foot level, talk a little bit about economic evaluations of genetic technologies, and then go over some examples to kind of give you an idea of what types of information you can get out of these types of analyses.

I guess the kind of message I want to get across is that cost-effectiveness analysis is not about just looking at cost only. It's really about putting a value on all of the things that we look at in health care, including quality of life and life expectancy, and really I think the advantage of formal cost-effectiveness analyses is that they provide a framework for evaluating the complex and conflicting factors that are involved in making coverage and reimbursements decisions in health care, and I think we all realize that with genetic technologies that's even more of an issue.

Another advantage that you can have here, and we'll see this as we go through the examples, we can look at multiple different strategies and many times, when we use modeling techniques, we can get information to decisionmakers when they're trying to make that decision, as opposed to years later.

I'm not going to go into all these different details here, but I just want to highlight that within this kind of area of economic evaluation in health care, there are a variety of different methods that folks use. A lot of times these are all referred to as cost-effectiveness analysis in general.

I think really kind of the gold standard in the field is what's called cost-utility analysis, and the reason that basically people like it is that you look at outcomes in quality-adjusted life years. So you look at life expectancy as well as the impact on quality of life in patients, and of course, costs are measured in typical dollar terms.

So one of the questions that was put to me was what information does cost-effectiveness analysis provide to health plans? Well, unfortunately, it's just one little piece of the puzzle, and I think as we've heard from the discussions today, there are a tremendous number of issues that go into decisionmaking. So I don't want anyone to feel like I'm advocating using cost-effectiveness analysis to make decisions about what to cover. It's just one piece of the puzzle, but I also think that it can highlight some strengths and weaknesses in these other areas.

Another tough question is is cost-effectiveness information used in reimbursement decisions in the U.S.? Well, I think we heard one perspective from Sean, and I can bring a little bit of another perspective on this issue, more from the managed care arena. The short answer to that question is

sometimes, and it's changing.

I think a nice example that's out there of the use of economic information in decisionmaking are the guidelines that have been put out by the Academy of Managed Care Pharmacy. These were put out and approved by the board of directors in October of 2000, and basically the objective of these guidelines for making decisions about pharmaceuticals were to improve access, improve the transparency of the information of the decisions, and try to achieve a consistency in making decisions, cover and reimbursement decisions about drugs to put on formularies.

Basically, what this format does is the managed care companies go to the manufacturers or the pharmaceutical and biotech industry, and they say give us all the information you have on your drug, including unpublished studies, and also provide us with evidence of cost-effectiveness.

So it kind of provides a framework for looking at this and it enables, when these decisions are made and when folks are making decisions in managed care, instead of just looking at one or two or three studies or the ones that have been published, you're able to have access to all of the information that's out there. There's obviously a lot involved with checks and balances and making sure this information is accurate and exhaustive, et cetera, but basically, it ends up giving the decisionmaker more information with which to make that decision.

So cost-effectiveness is a piece of that. The rest of it is really based around evidence-based decisionmaking.

This I think is about six months old, but the utilization of this format has become fairly popular. A lot of managed care organizations across the U.S. are adopting it, including a few of the states, and it's really become kind of -- hopefully, it's not a trend. It's the current kind of gold standard I think in managed care. There's a lot of other folks out there that have been doing this type of thing for a long time and doing it very well, such as Kaiser, et cetera, but there are a lot of smaller plans out there that really haven't been adopting a formal evidence-based evaluation as well as cost-effectiveness.

Just in our experience with running training programs, et cetera, when do you actually use cost-effectiveness information? Well, it's generally when you have, for example, more than one drug in a class of drugs and you're basically making your decision based on price, and so you may be wanting to look at things such as the cost of side effects and monitoring things like that.

I think the area where it draws the most attention is when you have an expensive and novel technology. So maybe, for example, when Enteracept came out for the treatment of rheumatoid arthritis. This is probably the situation where some genetic technologies are going to find themselves and this is when payers start to get interested in issues of cost-effectiveness.

This issue of do payers care yet, I think it's not quite on their radar screen yet. I think when you talk to them about genetic testing and pharmacogenomics, a lot of folks start to think, "Oh, biotechnology, biologics. Big budget impact. Now I'm concerned." So if it's something that they feel is high tech and expensive, they'll start to get interested.

I think in some of the data that Sean showed, it's not really having a big enough impact quite yet where at least folks in, for example, managed care have it at the top of their list. I think once we start to get more common genetic testing or tests that really influence the utilization of expensive drugs, you're going to start to see a lot more interest in cost-effectiveness of genetic technologies.

That's basically what I've covered here. Also, obviously, with regulatory intervention there would be greater interest also.

So what are the determinants of cost-effectiveness of genetic technologies and what makes something cost-effective? I just want to flip through a couple of issues here, just some work I've done with colleagues thinking about what could be important.

Really, for pharmacogenomics, there's a lot of information out there about drugs where their metabolism is influenced by genetic makeup in terms of drug-metabolizing enzymes, but you really have to ask yourself how serious are the side effects? Are they going to have significant patient impacts and economic impacts? If you're using pharmacogenomics to select a drug, is that an expensive drug? Is that something that's used over the lifetime of a patient? How much money are you going to save?

The same thing with disease genetics, looking at disease risk. You really have to consider what are the ultimate outcomes you're trying to prevent.

Another issue that I think that I've especially felt that in pharmacogenomics is often ignored is the concept of what's the next best thing? What's the comparator? What's the alternative?

So are you going to use genetics to decide which drug to use for a patient to treat their hypertension or do you just have them come back into the office every few months and over a six-month time period or a year time period, you get it figured out which drug works for them and which dose? That may not be too expensive, so paying a lot of money for an expensive test may or may not be worth it.

Of course, I think this audience here is familiar with the issue of association studies on the correlations between the genotype and the phenotype. A lot of the folks out there I've seen will focus in on test sensitivity and specificity as opposed to considering actual clinical outcomes in the patient and actual phenotype. Obviously, genes that have a higher penetrance will be more cost-effectiveness in terms of testing.

There are issues around the cost of the test. I think the presentations here today have covered a lot of this. There are things that we need to consider, such as the induced cost and additional clinic visits.

I think there are some benefits and potential benefits in genetic testing that does differentiate it from other types of diagnostics in terms of the ability to use that information throughout the lifetime of the patient. For example, this Roche amplichip, which looks at a series of drug-metabolizing enzymes. Basically, you can look at your entire drug-metabolizing profile on one chip. For instance, if you got that test when you were a young child, you'd have that information available to you for the rest of your life, and the cost is really kind of alleviated that way.

The last point is basically that genetic testing is essentially a screen or preventive medicine, and for those of you that work in that area, you know that cost-effectiveness is highly driven by the prevalence of the underlying disease, and in this case that would really be the prevalence of the genetic variant. If the prevalence of a genotype is only 0.5 percent, we have to go and test 200 people. So obviously, this is going to have a big impact.

We did a hypothetical cost-effectiveness evaluation of testing the TPMT gene, which Michele mentioned earlier, for childhood leukemia treatment with 6-mercaptopurine, and we basically

used decision analysis and built a decision model in terms of whether you would test or not and whether the patient was deficient or not and whether they had a serious adverse drug reaction and there is potentially mortality associated with that.

Now, this was just an example, so we kind of tripped this thing out, but basically we put in some parameters for the cost of the test, the mortality due to the adverse drug reaction, and then the prevalence of the deficient genotype. We found that these three parameters represent three of the dimensions in cost-effectiveness. The cost of the test, the economics; the genetics, the prevalence of the genotype; and kind of a clinical outcome.

What I'd like to show you on this graph here is basically what we've done here is plot -- this is the mortality associated with the adverse drug reaction, that's the cost of the test on this axis, and on this axis here we have what's the incremental cost-effectiveness ratio. Basically, just to make this simple, things that cost less than $50,000 per quality-adjusted life year in the field is somewhat considered reasonable and cost-effective. When you're between 50 and 100, not quite so. It's more of a question mark, and then above 100, it's generally not considered cost-effective.

So in this example, when we're using the default prevalence of the genotype of 0.3 percent, you can see that depending on these other parameters, you may or may not be cost-effective. It may not be a reasonable way to spend your money compared to other interventions that you could be allocating your budget to.

But when we change this from just 0.3 percent to 1 percent, you can see the significant impact it has on the cost-effectiveness. So even small changes in the prevalence of the genotype can have a big impact, even in terms of budget impact in terms of the number of people that you identify.

Now, I just wanted to give you guys a few examples from the literature. This is a study published recently, November 2003, looking at newborn screening for MCADD, and this was using a tandem mass spec technique. Just briefly, basically what they did was they created a cost-effectiveness model using decision analytic-type techniques, like I just showed you there, and they did a cost-utility study. So they were looking at cost per quality-adjusted life year.

They assumed the cost of the test was only an additional $4. This was assuming that there was already some type of tandem mass spec testing going on, and they looked at what would happen with screening versus no screening in looking at the 2001 birth cohort.

Well, they found that you'd end up with longer and better lives. So you'd have a gain of 990 quality-adjusted life years. So let's just say 1,000 life years is what you'd save.

You would have, however, a higher overall cost of $5.5 million, but if we convert that into the cost-effectiveness language, we end up with $5,600 per QALY, which is a lot less than the $50,000 per QALY. So this might tell a payer that this is a reasonable technology to reimburse.

If we look at colon cancer, there's been some work in this area. Scott Ramsey has looked at testing for HNPCC, and again, I think Sean outlined this nicely. Basically, what they found is that the incremental cost per QALY is about $40,000 per QALY if you look only at the patients, but when you include family members, the siblings and children of those patients, all of a sudden you get tremendous more gain for the amount of money you've spent. I think that might have interesting implications in terms of who's covered and who's reimbursed for genetic testing and obviously can run into some difficult reimbursement issues.

I think there is also some interesting information that's come out of some of these studies where some folks have advocated universal screening as opposed to folks that fit within the Bethesda guidelines, et cetera, and have found that the cost, the annual cost, in the United States could be pretty dramatic if we were to end up full testing on all patients.

Breast cancer. There's been not as many studies as you might think of the cost-effectiveness of actual screening, but Grann and colleagues have a study looking at Ashkenazi Jewish women, and again, not to go through all the details of the disease, basically what they found was that for a cohort of 10,000 women, you could avert about 80 deaths by having this screening program. They found in their calculations that you were doing this at a rate of about $30,000 per life year saved, so something that seems very reasonable.

However, they conducted that analysis with a default value for the test of about I think $400, and when you plug in something perhaps a little closer to what might be reimbursed, now you're up in the $85,000, pushing $100,000, per QALY. So a payer might utilize an analysis like this to give some pushback on the cost of a test or try to negotiate on the cost of a test based on its value.

Now, does this happen every day with the Academy of Managed Care Pharmacy guidelines? No. It's a much more subtle effect, I think, but it provides a framework for these types of negotiations.

Then lastly, for pharmacogenomics, this is some work that Katherine Phillips, a colleague of mine from UCSF, has led. It's actually working with the FDA, doing some work with them. She did a systematic review looking at cost-effectiveness studies of pharmacogenomics.

Basically, just to sum up, she found 10 studies out of a total of 253 citations that were identified. Four were in thromboembolic disease, a couple were in chronic hepatitis C, two were looking at the enzyme thiopurine methyltransferase, and a couple in other areas. Eight found that genotyping was relatively cost-effective, while two studies found it to be less cost-effective than other options. So that's kind of the landscape of what's out there for pharmacogenomics.

I'll skip this slide.

So what are some of the unique challenges of looking at cost-effectiveness of genetic technologies? I think a lot of it is fairly obvious. Basically, there's a lot of information, it's complex, and it's interacting, and so there are pretty significant data needs.

I think some of the things that need to be worked out are what are really the induced costs surrounding testing. A lot of these issues of the cost of adverse drug reactions, for example, I don't think have been costed out very well, and the whole issue I think of patient preferences and quality of life needs to be looked at a little bit more closely.

You know, I feel that using a decision modeling framework, you can kind of bring all these complex factors together and with additional data in these areas in the economic outcomes, the patient outcomes, as well as obviously, as the committee discussed earlier, the clinical outcomes and association studies, with this type of information I think it is possible to provide useful cost-effectiveness information to decisionmakers.

So along the lines of what I think everyone's been talking about and thinking about are providing some types of guidelines and policies for the reimbursement, using an evidence-based approach, and incorporating some aspects of cost-effectiveness into the process.

I think some issues that I've seen will be who will be responsible for these decisions. Is it going to be the P&T committees or medical services? I think for pharmacogenomics, it may very well be that it falls under a P&T pharmacy services area.

I think there's particular interest with regard to pharmacogenomics in terms of it's a real pain for them to try and control drug use by requiring prior authorization, but if a drug comes with a genetic test that's required, it kind of makes them easier to control drug utilization and expenditures potentially.

So in summary, I think cost-effectiveness evaluations in health care is challenging to begin with. I think in genetic technologies, it's probably one step further.

I think because, however, the decisions are so complex and there are so many factors involved, that decision analysis and cost-effectiveness analysis at least provide you with a framework and it can highlight where your data uncertainties are and where additional resources need to be invested.

I think that as more tests come to market, that the need for these types of studies are probably going to be increasing as payers are faced with more decisions in this area.

So that's it. Thanks.