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Presenter: Ciaran Phibbs

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Dr. Ciaran Phibbs: I am Ciaran Phibbs; I am one of the economists at the Health Economics Resource Center. As Heidi said, this is part of our cost effectiveness course, and the focus here is on something that the Public Health Service Panel referred to as the Reference Case and we are going to go through that. As she said in terms of questions, if you have questions, we have someone monitoring the questions and Todd will make a decision as to whether to interrupt me or defer based on the nature of the question. So if you have a pressing question, you have to use the question button.

Just in terms of the objectives of the course – the items are: Why do we need to standardize cost effectiveness analyses? What needs to be standardized? And note that this is building on details from the previous lecture. Putting out the reference here, that Public Health Service came out with references in terms of cost effectiveness twenty years ago now. I will note that these are in the process of being updated. I am not sure exactly when they are going to be released but this is sort of the Gold Standard if you will in terms of the methods, there have been other references subsequent to this that have built upon these standards, but this is the basis of it.

I will also note that and have provided three references here if you do not want to slog through the whole book, there was a series of three articles in *JAMA* that have the gist of it if you will in terms that boil down the key findings in a more concise manner.

Before we go on I just want to understand the audience, I have a quick poll. Have you ever conducted a cost effectiveness analysis? And there are three possible answers: No; one study; more than one study. Heidi will open up the poll.

Heidi: The poll is open right now, responses are coming in. I will give everyone just a few more moments to respond before we close this out.

Dr. Ciaran Phibbs: Obviously those of you who are on the phone cannot answer those.

Heidi: But for those of you who are in the session, it looks like things have slowed down so we will go through those. What we are seeing is seventy-seven percent saying no, they have not; seventeen percent saying one study and six percent more than one study. Thank you everyone for participating.

Dr. Ciaran Phibbs: Okay so most of you have not conducted an analysis and that is important just from a perspective of my analysis. Why do we need cost effectiveness analyses? Just conceptually and Risha addressed this somewhat last time. Again, if you think about it healthcare interventions affect many different outcomes in many different ways. The idea here is that cost effectiveness analysis can give us a common metric to allow comparisons across diverse diseases, conditions and patient populations. As a hypothetical example we can compare the valuations for the value of interventions for PTSD compared to coronary artery disease and that is relevant because in terms of this cost effectiveness or cost utility analysis I will talk about, that PTSD does not have as much of an effect on mortality as coronary artery disease, but it certainly is affecting quality of life. By denominating things in terms of quality adjusted life years you can get a comparison between these two very diverse interventions or conditions. That is the idea that with all of these different conditions and things that composes all of healthcare that it is a metric that gives us a common metric that we can compare the value of these interventions as a way of helping to allocate scarce resources.

In terms of that we have cost effectiveness analysis tool for decision-making as I said previously a common metric for diverse interventions and the normal thing is that an intervention or treatment is compared to an alternative which is usual care. This is different than what happens in drug trials. In FDA approved drug trials you compare the effectiveness of some new drug compared to a placebo and that will overstate the gain of that drug because in absence of the drug unless it is a drug for a treatment for which there is no condition, you would not be treating the patient with placebo you would be doing something else. So in terms of evaluating, looking at the evaluation of an intervention you want to compare it to what the patient would otherwise get.

Another word to think about is is the treatment or intervention better than the current standard of care and that is the relevant comparison that one really wants to make. It is not – is it better than doing nothing, but is it better than what we would otherwise do?

In terms of this, to do this you need to find both the cost of the intervention and of the comparator or usual care and assign values to the outcomes. The outcomes need to be measured in a single scale, this goes back to the point I just made about being able to compare diverse conditions which one condition may affect quality of life more than mortality and so on. The standard that we use here is quality adjusted life years. There are other standards, in international things you see something called DALY’s or Disability Adjusted Life Years, similar concept that we are trying to adjust quality adjusted life years is more than just disability and includes other metrics. We are trying to generate a common metric so we can compare these diverse interventions.

I just want to note and Risha brought this up last time, is the labels of cost effectiveness versus cost utility analysis. Cost utility analysis is a specific form of cost effectiveness analysis where the outcome is measured in utilities. It is more generalizable and you can do a cost effectiveness analysis where you are just looking at not a quality adjusted life years but at a common metric like mortality or something that is not as generalizable. I am going to apologize in advance because I am older and when we used to refer to cost effectiveness analysis thinking of what people refer to now as cost utility analyses. So I am going to use these terms interchangeably but this talk is really about what is formerly called cost utility analysis.

There is something called Dominance Principles that is the only tool available where outcomes are not measured in qualities. What you are saying is if you do not use these quality adjusted life years, you can say – is the intervention more favored if it is effective and costs less. That is what is called a dominated or a dominated intervention. In some literature they refer to these as cost savings. The intervention both improves outcomes and costs less. Just to apply an algebraic principle you can have extended dominance of A’s. If A dominates B and B dominates C, then A is going to dominate C.

Let me pull up here, something weird happened here. I was trying to get the spotlight on and my slides disappeared Heidi. What happened?

Heidi: We have a black screen here, are you able to undo it?

Dr. Ciaran Phibbs: Yes, I am going to go back to normal.

Heidi: It looks like something here, a video card or something is not…

Dr. Ciaran Phibbs: I got the slides back.

Heidi: No we still have a black screen here. Okay, there it is back.

Dr. Ciaran Phibbs: Okay, I am not going to be able to point, if you are seeing my screen, can you see my cursor moving around here.

Heidi: We can yes.

Dr. Ciaran Phibbs: Okay. Basically if you think of cost effectiveness and you have a plain and you consider the changing cost – is it higher cost or lower cost and you consider the change and effect of it. Is the intervention less effective or more effective? In the upper left corner you have where the intervention is dominated by standard care, and that is because if you evaluate intervention and it is more expensive and less effective you are not going to do it, it does not make sense to, that is clear. Down in the lower right corner you have where the intervention is preferred which means it dominates standard care and that is because it is saving money compared to standard care and is more effective. The question areas are the upper right and lower left quadrants where in the upper right you have something that costs more and is more effective and we are asking – what are we getting for that additional cost, then you have the opposite if it costs less but is less effective. As comparing in terms of – is this intervention worth doing? Is it worth the extra expense?

Todd: Ciaran.

Dr. Ciaran Phibbs: Yes.

Todd: We are getting, one person says the audio is not connected. I am hearing you fine but I am not sure if that is a delay in the system. Heidi are you having any problems?

Heidi: I am not having any problems. I am assuming that they are on VOIP so I am going to send them a message quick, they may need to disconnect and reconnect.

Todd: Okay.

Dr. Ciaran Phibbs: Okay. Sorry about that. Anyway the thing is that most interventions when we do a new intervention they are in this upper right corner and it is more expensive and we are getting better outcomes. Than the question we are trying to determine is – are the outcomes we are getting, are the gain and outcomes that we are getting worth the additional costs? Dramatic improvement in survival or quality of life and it only costs a few pennies it is a no brainer – yes we will do it. Same thing, trivial gain and outcomes and it costs ten billion dollars per patient of course we are not going to do it because it is just far too expensive and not worth that added investment and it is where do you make those cut points.

I want to emphasize because everybody thinks about in terms to continue that point is that strong dominance or cost saving when you have better outcomes and lower costs relative to the universe of medical interventions, these are rare, there are not many of them. These are the no brainers, yes of course we are going to do it, and it saves money and is more effective. There are not many of these no brainer decisions which is why we need to do the more careful analysis. Just as some examples many if not most childhood immunizations or vaccinations are cost saving in that they save money and improve outcomes the polio vaccine, MMR vaccine, etcetera. Age appropriate cervical cancer screening meets these criteria; mandatory motorcycle helmet laws meet these criteria. Just to take that last one, helmets do not cost that much and you are preventing really traumatic injuries that are very expensive and deaths. The net savings exceeds the costs.

I am going to talk more about specific examples that will help explain why this is so rare. This is in 1990 in the U.S. I know this is not a VA relevant example but it brings up a lot of good points. Neonatal surfactant replacement therapy was approved, surfactant is the gummy substance that maintains the surface tension in your alveoli so they do not collapse when you exhale. We all have it, if we did not we would be dead. Many premature infants do not have this naturally; they have not started producing it yet. This is an artificial one, they intubate the baby, you spray it into their lungs, and you get dramatic improvement and lung function. It halves the mortality rate for these very preterm infants taking it from a baseline of about twenty-five or thirty percent down to twelve to fifteen percent. This is a huge gain in effectiveness and what is in terms of cost, the thing that you have to remember and premature newborns are an extreme case of this and most of these kids if they were dying were dying in the first two days of life and they are now going to be in intensive care for their range of prematurity until they get to about term. Increasing survival is something that is really, really expensive. This therapy actually ended up saving money and I did some of these early analyses which is why I know about this in such detail and that is remember the baseline mortality rate was only twenty-five percent so most of these kids were surviving already and being very expensive. Because we treated the underlying disease, we dramatically reduced the treatment intensity and the length of stay that those who would have survived anyway. That savings paid for this extra ten to twelve parents of babies who are now living and having those much higher costs. You have that net mortality, reduction mortality and lower costs and I just want to point out that this highlights the reason why interventions that improve outcomes frequently do not save money and that is because you have this intervention that is improving the outcome but because of that the patient is going to incur a lot of extra costs. It also highlights something that we may see a change in and I have an unnecessary space in that last point and basically this was a biotech developed solution. We have an artificial drug that we are giving to the patient, it treats the underlying biologic problem. The underlying problem was the deficiency fact and we provided an artificial surfactant that solves the underlying lung function problem and that is where you are getting the dramatic difference. As the biotech revolution evolves, we may get in dealing with the underlying biology we may get more treatments that are cost effective. A more current example, I do not know where it actually falls out in the cost effectiveness spectrum given that Gilead has priced it so high. The new Hepatitis C drugs certainly deal with the underlying they cure the disease so you do not have these long extended costs plus mortality and disability. If they were priced more reasonably that would certainly be a cost savings. I do not know where it stands now, I am sure they have done the analysis so it is in the cost effectiveness region just because that will maximize their products but I cannot speak to that.

To come to what we do in terms of, and Risha alluded to this the way we express the results is what we call the Incremental Cost Effectiveness Ratio or ICER. What we are doing is we are comparing the way we report these results is the added cost compared to the added gain. You take the cost of the intervention or experimental treatment compared to the cost of the control which is going to be usual care and compared to the qualities so you are getting – how much more does it cost us and how much more do we gain. If that number is positive we are going to have added costs and if we get a gain in quality so we are going to have more cost, more quality. What are the costs for quality? Is it going to cost us ten dollars for additional quality or a hundred dollars for additional quality?

You see here that there is this standard, and I will get back to this, that is somewhat arbitrary that the cost per quality of fifty thousand dollars per quality is the standard and so as the effectiveness goes up, and so you have this line and are you above or below that line. Interventions that are more expensive, standard of care is preferred; if you are below that intervention is preferred.

Where does this fifty thousand dollars per quality threshold come from? I want to note that it is both old and arbitrary. Basically many years ago now, Medicare was extended to cover end stage renal disease. Someone did a quick estimate that the gain was about fifty thousand dollars per QALY; they rounded it off and said – because the public has voted to contribute tax payer dollars for this intervention the public is willing to pay fifty thousand dollars per QALY. A few things – one is that this number has never been updated for inflation and the costs are certainly higher now than they were. The other thing is that this really, one could question as to whether this was a valid measure of the public’s willingness to pay because – a; it was a political decision and there were a lot of special interest politics involved and one can certainly argue that this was not necessarily an accurate representation of the public’s willingness to pay. I will just say that as a result this is sort of sitting out there in the literature as an arbitrary standard; some people are saying because we have not adjusted for inflation it should be closer to a hundred thousand. Other people are saying we really do not know and what we should do is just put the numbers out there and reflect public’s willingness to pay. I just want to note this is an arbitrary number but it is a standard that many people use.

What is the reference case and why do we care about it? This is what the Task Force referred to as the reference case and why is it important? This is the standard set of methods and assumptions that serves as a point for comparison across studies. Why is that important? If you think about it, if I did my cost effectiveness analysis one way and somebody else did it another way, and you made all these arbitrary decisions, the disadvantage of that is that you would not be able to compare different studies and that would greatly reduce the value of that study. If Study A used one set of methods and assumptions; Study B uses a different and did not standardize you really cannot compare those two studies so you do not know what the cost effectiveness is of the different treatments. By using a standardized or reasonably standardized set of assumptions and methods, we are able to compare the cost effectiveness of all of the different studies for which a cost effectiveness or cost utility analysis is done. It greatly increases the value and this is why in many journals when they try to publish a cost effectiveness or cost utility analysis they ask you to go through these various checklists and different societies have come up with checklists for reporting cost effectiveness or cost utility studies. They are asking do you comply with these and the reason that they are doing that is that if they do you can then really legitimately compare Study A to Study B.

Just some of the key assumptions and we are going to come back to these in some detail is that you adopt the perspective of society which is sort of a global perspective. In the VA we may also consider what the perspective of the VA, but there can be external costs on other family members, costs imposed on other insurers, Medicare, Medicaid, etcetera. You need to consider all of those as the recommended thing. In terms of measuring cost, you are to measure the direct cost of the intervention; and all healthcare expenditures and patient and care costs and to express the results in quality adjusted life years. We are going to talk more about these in detail.

All health effects are to be in the denominator and the numerator is to capture the changes in resource consumption associated with the intervention. You are to discount all costs and outcomes at a three percent annual rate. It is not an issue now, but sometime ago when inflation rates were higher, people were saying – inflation is higher than that. And the fact is that three percent represents the long term average return to capital which is a measure of the real return if you will. That is an appropriate real discount rate and the advantage of doing is by doing this if you were to use a nominal interest rate you then have to project out what inflation is going to be and you are imposing a lot of errors into your estimates in terms of the variants. So by using this you are doing everything in real costs or inflation adjusted costs.

You may need to model the effects of the intervention not fully realized during the study period. For example, many cost effectiveness analyses are done in conjunction with a clinical trial and the clinical trial runs for a finite period of time. But if you look in terms of the effects of the intervention it can well have effects of the intervention that extend beyond that study period both in terms of cost and in terms of outcomes. So you need to then do models to project how those effects extend over time and you use the literature and so on and that will be topics of future lectures in terms of how to do that. You need to conduct sensitivity analysis and that is because there are assumptions built into any of these especially in terms of the modeling. There are assumptions built into the analysis and you need to test the validity of those assumptions and figure out which ones and report which of the assumptions have real effect on the analysis versus which ones the results are not sensitive to. You need to detect statistical significance of the cost effectiveness of the findings and adhere to the standards of reporting as I talked about earlier.

Coming back to adopting the societal perspectives, as I said I am now cycling back into some more of these details. I alluded but the payer perspective may yield very different results because of the benefits and costs occurring to others, both the patient, other payers, family members, employers. By using the societal perspective you are considering all of the costs and all of the impacts. I will note that it may be useful for studies done within the VA to also do a study from the VA perspective because this can inform and be more useful to managers in terms of trying to make the decision because the VA being a fixed budgeted system they need to consider the impacts to the VA and that will have an influence on management decisions. VA managers are appreciative if you can present the study results if you also do analyses from the perspective of the VA.

Particularly and this again is going to be the topic of a future talk but what are called budget impact analysis is something the VA managers are particularly appreciative of shall I say. In that because it provides them with the information about the cost of implementing an intervention; what the timelines of the cost and benefits and it is important for budget planning. If you have an intervention and you find something that is cost saving but those cost savings are down the road, in a fixed budget system you need to account for the fact you are going to have added expensive upfront and by providing VA managers with the information about okay what is the timeline of those costs and savings, and spell it out, it is more useful for them in terms of doing that and it may also help speed implementation decision or an adoption decision if you can provide this information. They then are less skeptical of the results sometimes.

In terms of we have that incremental cost effectiveness ratio in terms of what goes up in the denominator versus the numerator. All effects are supposed to be in the denominator and expressed as QALY’s. The numerator of the cost effectiveness ratio is supposed to calculate the changes in resource assumption associated with the intervention. The thing that you need to be careful about is that there are things that are considered gray areas that could be placed in either and you need to make sure that you avoid double counting.

I believe this is the next poll here in terms of asking – do these belong in the numerator of the ICER? Yes or no answers and the options are: healthcare costs associated with the intervention; the length of stay; the costs of patient time; and the value of lost productivity. If you will give me answers in terms of yes or no do you think the costs should be in those and we will talk about those. Are people answering?

Todd: Actually I do not see the poll yet so Heidi can you put the poll up if you have a chance.

Heidi: My apologies it is coming up right there.

Todd: Okay.

Heidi: For this you can pick all that apply so that we can get an idea of what all people are thinking should belong in that numerator. Responses are coming in a little bit slower here but people are needing to read through and make those decision so I would expect that to be a little slower. We will give everyone a few more moments before we close this poll out. We are just about at fifty percent, give everyone a minute, thirty seconds or forty seconds more before we close this out and go through the results. It looks like we have slowed down significantly so we will close this out. What we are seeing is ninety-three percent saying healthcare costs associated with the intervention; fifty-seven percent length of stay; seventy percent costs of patient time; and sixty-two percent the value of lost productivity. Thank you everyone.

Dr. Ciaran Phibbs: Okay so the answers in reality is: yes / no / yes / no because length of stay, virtually everybody got that healthcare costs associated with the intervention, what you are doing, you should count those costs – yes. Length of stay is part of that cost if there is a cost. The cost of patient time and the fact that is a cost of the intervention, the fact that the patient has time and the value of lost productivity, the reason that is not in there is that should be captured in the QALY. The other thing that you note is that measuring specific costs like that if you measure productivity costs you cause a bias because children and those that are retired or disabled do not have lost productivity so you bias interventions against them, that is another reason.

Coming back to the components belonging in the numerator, you are considering the costs of the healthcare services that is there; the costs of patient time and the reason you are counting patient time and valuing time in standard units is that that is a real cost and you cannot be doing something else. That is the cost of patient time for the intervention not the lost time to sickness, etcetera, it is the patient time for the intervention and the fact is is that different types of care require different amounts of patient time and that is why it is in there. The cost of caregiving whether paid or unpaid, other direct costs such as travel time and you use costs measured in constant dollars and you use wage rates to value time costs. By doing that and using a standard average wage rate you are applying that patient time regardless of whether the person is working or not you are not measuring lost wages you are just measuring time times a standardized wage rate.

More components that should be in there – there can be non-healthcare costs in there such as costs of criminal justice. If you have a drug treatment program for example for heroin addicts who tend to have, not all of them but some of them, will use crime to sport their habit and if you eliminate that associated crime that is a very real gain or reduction in cost and should be in. You need to include costs imposed on others, think of the criminal justice as an example but it is a cost where there is, because of this intervention you are imposing an additional expenditure or eliminating an additional expenditure as a result of the change in the outcome. Do not include lost productivity as this effectively is a double counting because that is embedded in how QALY’s are measured. I am not going to go into the details of how QALY’s are measured but when properly measured quality of life embeds the productivity effect including wash productivity in the numerator would result in a double counting and bias the results for those that are more effect working age adults. Note that in terms of an employer making decisions, they may consider how the health affect affects their productivity but that is not what should be in the standard reporting that we want to be able to compare these interventions across a lot of interventions.

\_\_\_\_\_ [00:37:22] out here in terms of the recommendations, you have healthcare costs associated with living longer. The recommendations are that you include the costs for the intervention related diseases within the original expected life span without the treatment and for any added years of life. So if you do an intervention for treating coronary artery disease you would include the costs related to treating coronary artery disease during the previous expected life span and for any added years. You include the cost of treating adverse events. The standardized recommendation is to exclude unrelated healthcare costs and non-healthcare costs within the expected lifespan and exclude non-healthcare costs for the added years of life. The panel made no recommendation for unrelated healthcare costs for the added years of life.

That is the official recommendation. I will note that this particular set of recommendations is exceedingly difficult to imply and you have to make a lot of assumptions. And many studies do not try to slice and dice these costs and just look at all healthcare costs. When you get outside the realm of a clinical trial and you are starting to do modeling then it is somewhat easier to try to make these distinctions, but even there you have a lot of assumptions and it is very difficult. This is an area where there is a lot of non-compliance with formal recommendations shall I say in terms of just studies considering all healthcare costs simply because it is really difficult as you are projecting into the future to make projections about what healthcare costs are related to the intervention versus not related to the intervention.

I am going to move down to the denominator and as we have noted many times, we measure the health effectiveness in QALY’s and that the QALY should be preference based. Preference based and the weight should be based on community preferences and you should use a generic health-state classification, as opposed to disease specific and to use age- and sex-specific health related quality of life to value the gains and loses. These are just a generic set of recommendations and to come back in terms of these – why do we want to use a generic health-state classification as opposed to disease specific? Because for many diseases there are disease specific measures of quality of life and we do not want to use those, we want to use the generic one because the disease specific ones you cannot compare across other interventions.

I have been involved in many trials where I have in many other trials will also look at disease specific indicators of quality of life simply because those give you a better idea of how your intervention is affecting the things that really matter for that specific disease. It is useful information in the context of the trial but you do not use it for your cost effectiveness analysis. The other thing is the weight should be based on community preferences and there actually is some debate about this but this is the general recommendation in terms of how society values different outcomes and the way these are listed is you ask people questions and what they are willing trade off and it is not people with that disease. I will not go into the details, this will probably be addressed in terms of when we talk about utility reference, but there are biases that can creep in in both directions in terms of asking people who actually have the condition to rate their quality of life. They just in general, I will note, that people living with conditions tend to rate them that are chronic conditions or serious disabling conditions, tend to rate their quality of life better than the community ratings sort of saying that the community may not be able to perceive or think those insults are worse than they actually are. The flip side is that for many of these conditions the person may not have the perspective of what it is to have full health. There are biases in both directions, there is some debate on this. I am just noting that these are the recommendations; this is how the journals want you to do it so you have a standardized method that can be comparing across disease states.

I noted before just alluded that modeling may be necessary. Most clinical trials do not cover the full time horizon of the potential affects both in terms of costs and QALY’s. Most trials follow people for a set period of time, not until they die. It is allowable to use modeling and data from other sources to complete the analysis and the use of expert judgment should be avoided. In other words, use data to make these assumptions for okay what is the quality of life going to be like projecting on out until death and what are the cost extremes going to be like. You can conduct sensitivity analyses on these as opposed to just pontificating.

I already talked about the discount rate, what you should use the real discount rate of three percent and then what you do is because you are using a real rate you need to use real dollars. For your study period you adjust everything for inflation so you have real dollars or inflation adjusted dollars. From your time periods you go on out, you want to discount both the costs and the outcomes. You can conduct sensitivity analysis in the discount rate especially with long time horizons, things get very sensitive to changes in the discount rate but three percent is the recommended rate.

Conduct sensitivity analysis. If you have made assumptions or even if you have a clinical trial and you have complete things and you have not made any modeling assumptions, but it is a relatively small trial, you could have variants. So you want to see, understand what types of affects can have a big effect on the analysis. You have an intervention where you have some device that you are using or some new drug and you have the cost of that drug, well, there are pricing policies behind that. I alluded to the new Hep-C drugs and if the price were lower, given they are so expensive, if they were half the cost you would dramatically change the cost effectiveness ratio. This is one where given the prices of those drugs the ICER may be quite sensitive to the price of the intervention. What you want to do is for all of the key components that are feeding into this ICER you want to see how sensitive the results are to changes, varied in the results one way or another by one standard deviation is a common thing. For interventions like drugs you might say well what if we have the price of the drug. Use common sense to figure what is the price of the assumptions and you should do this both in terms of one way analysis and also conduct multivariate analysis. What happens if I change A and B, how does that change? What you really want to know is how robust are these findings and if they are not robust what things are the results particularly sensitive to because that makes the results much more useful from a policy perspective.

When you have results from a trial it is recommended that you use Bootstrap to determine the cost effectiveness ratio. What this means is if I have done a trial and I have all my data, and I have the data on the change in costs and the change in outcomes of each individual in the trial. Then what I do is the trial determines my sample size and I just randomly sample with replacements from that pool of samples and get a cost effectiveness ratio. Then I repeat this a thousand times. The percentage of the replicates that are not cost effective is essentially your p-value.

This slide just shows, I just picked this up from a colleague that shows changes in survival and changes in costs. We see actually most of these are in the lower right quadrant so you have an improvement in survival and lower costs which would be dominant, but not all of them are and not ninety-five percent of them. It is tending towards costs savings, but it is not clearly that way, you have some cases where you have an increase in survival but increased costs and some you have reduced survival with reduced costs. You even have a few where the costs are higher and the survival is worse in terms of the outcomes so it is not totally clear that it is thing but the evidence is certainly pointing in that direction and the point estimate for this trial will certainly be cost savings just not significantly so.

The p-values are sensitive to what your threshold is for what you consider something cost effective I just want to note that and there is this whole idea of willingness to pay. I am cycling back, there is *JAMA Ray* paper, and ISPOR also has a newer set of recommendations for standard of reporting them. As I alluded to before it is important from a policy perspective. I just want to mention an alternative to reporting the ICER is what is called a net-benefit regression and I put the reference in here. The thing is the ICER gives you this ratio and it is a ratio of one number to another and you have to do the sensitivity region. This method is essentially a regression-based test and you get a direct test of the statistical significance. There was a HERC Cyberseminar by the first author of this paper, I put the date that should be archived if one wants to go find out more about that method.

I alluded that there are some other references so in the slides I put some of the other references and there is some stuff that should be updated about this that I have not included here, I apologize in terms of the ISPOR standards. Never mind, yes they are, here they are. These are just other references about things that you should consider in terms of reporting.

The next seminar is in two weeks; Todd Wagner will be talking about “Estimating the Cost of an Intervention”. Are there any questions Todd?

Todd: I think we confused everybody sufficiently but there are no questions yet, but hopefully they will write in [laughter]. There was one question that a person had again about the handouts Heidi, I just to point you to that.

Heidi: Yes I just sent that link out to everyone so they should be seeing that very shortly.

Todd: If other people have questions now would be the time to send them in. Thank you for your presentation Ciaran. One person gave you a compliment Ciaran, says no questions but thank you it was very helpful. You did a great job setting up the scenario for the talk so hopefully people will come to the remaining sessions and if they have specific questions we can address them there.

Dr. Ciaran Phibbs: I mean as you may have gathered from previous lecture and this lecture just sort of setting the background and subsequent lectures are going to talk to the details about doing the different components of doing a cost effectiveness analysis.

Todd: We do have a few questions coming in. Do you need to calculate the costs for each participant?

Dr. Ciaran Phibbs: The normal method is that you would take, there can be averages, for example, let us say the intervention is a counselling intervention and these counseling interventions vary and have somewhat different costs because some take slightly longer. But it would be really expensive in the trial to try to measure the number of minutes of each of these interventions. What you do is you figure out what the average is and you just apply that and you have to be smart about this. That is going to be relatively small cost probably in the big picture of things and for that kind of thing you can use an average. I was involved in a trial that involved the patients using a home monitor for monitoring their INR for patients on Warfarin. The patients would have to call in at times to the nurse managers and instead of having the nurse manager or the nurse coordinator have to write down how much time they spent for each patient when they called, what we did was we said on average how long does it take. They gave us a number of five minutes or whatever it was and we costed that out. But the thing is in this patient because this is a patient population where the patients are at serious risk for big medical costs. Whether we measured that at five minutes or ten minutes the difference was going to be very, very small compared to the total cost so it really was not going to matter but we wanted to make sure that we are capturing something. For those types of things it is okay to use an average, but for the rare events that are costly, things that are going to drive the results you definitely want to be capturing the actual costs incurred.

Todd: Just to back up one level if I may Ciaran, we do at HERC a lot of cost analysis alongside a clinical trial and that is what Ciaran described where you would actually calculate the exact costs of the patient level and then develop averages. There are people who use software like TreeAge to develop models of cost effectiveness and they will use published data or expert opinion and use point estimates as best they can with standard deviations so it may not be specific and they will do a lot of work there in just the modeling. Doug Owens work, Jillian Sanders work for example are two well-known people who do those types of models where you may not have data at the patient level.

Dr. Ciaran Phibbs: Yes, when you do that it is especially important to do sensitivity analysis on those numbers.

Todd: Correct. One clarification used in some sense that terms cost effectiveness and cost savings, and you mix those terms, and they were used differently in the previous lecture. Yes do you want to say anything to clarify. I think the cost savings term that you were saying was much more of a dominant issue.

Dr. Ciaran Phibbs: Yes.

Todd: Still assuming that one was preferred quality-wise really equal quality-wise. You could have a study that is purely just looking at cost and saying this is cost savings without any information on the quality or outcomes sort of like a cost minimization study.

Dr. Ciaran Phibbs: Yes. Cost savings is a particular term in terms of the ICER that means that it is both more effective and less expensive.

Todd: There was some confusion when you got back into your poll about length of stay and why you excluded that. I think that people got confused because when you include the cost of the intervention that intervention may not include healthcare. I think where you were assuming that it included all the healthcare including what would be the costs associated with length of stay.

Dr. Ciaran Phibbs: Yes.

Todd: And just did not make that clarification.

Dr. Ciaran Phibbs: The length of stay should be measured, the length of stay you are not going to put in length of stay because that is not a dollar denominated thing, and you will measure that in terms of the cost of the hospitalization.

Todd: Correct, I just wanted to clarify that.

Dr. Ciaran Phibbs: Yes.

Todd: There was some confusion and some people said – no, no, I want that, you definitely want those dollars in there, but you…

Dr. Cirian Phibbs: The dollars associated with hospitalizations have to be there but you are putting it in as dollars but not length of stay.

Todd: Yep. Then in the scattergram how do you accommodate very high cost outliers?

Dr. Ciaran Phibbs: What happens there, I think there are two different points? In terms of that scattergram what that is is you are taking all the points in the trial and you are sampling with replacement. So a high cost outlier is included or excluded maybe driving how the ICER shows up because in one random draw that high cost outlier could be in there three times and another one it could not be in at all. That will give you your variants. The point is high cost outliers are real patients that you have occur at some low probability. So whether you have one of those in your study or two can really affect it,. If you just look at the mean and that is why you want to do this sampling with replacement to give you a better idea from a clinical trial relatively small samples what things really look like in terms of the risk of the distribution being where it is.

When you are actually looking at data in terms of a trial you may want to use common sense. I did a trial many years ago where there was one patient that had a cost of $1.3 million and then the next most expensive patient was something like three hundred thousand. I will not go into the clinical details, but I mean this patient was like a one in three million type patient, just exceedingly rare, you do not expect to see these, maybe even rarer than that. It was just a totally off the chart type of outlier so we excluded that patient. Actually that patient was a control so it made our intervention not look as good but we felt that we had to do that because that one patient was significantly moving the mean cost of the control population. That is the only type of extreme outlier that I would put in there, something that is just exceedingly, exceedingly rare. Otherwise just the high cost outliers that occur with some regularity those are real costs and in different populations you can get more or less of them and you want that to be reflected.

Todd: There is a question about – is there a way to apply CEA at the patient level and then I assume that current methods are based on population data.

Dr. Ciaran Phibbs: In terms of you can clarify but what I think the person is asking is okay is it cost effective to apply this technology to Patient A so some specific patient. The thing that you have to remember cost effectiveness analysis is designed to assess the value of an intervention on average for a defined population. There will be patient specific differences and there are a lot of variants and the idea is that this is really for setting policy about – are we going to adopt this intervention – yes or no. Not that it does or does not have value to a particular patient. It is the case that for many interventions they are a great value for patients that are high risk and obviously of no value for patients that have no risk and it is where do you draw that decision. And this is to help inform that but where an individual patient is going to be based on where they are in that risk factor. Does that confuse things or Todd do you have any clarifying? I am making a conjecture here.

Todd: It is a little unclear what the person says. The person says – be careful with what you are perceived as a rare event, you may have a rare event at your hospital that you only see as one case per year but if you look at it system-wide there may be four hundred of these similar cases, that is not rare. It depends I guess on what the denominator is there so it is still unclear exactly what is rare.

Dr. Ciaran Phibbs: Yes, I mean in terms of my excluding that rare event I am talking about this was on a population perspective from the State of California as an event that would occur in the order of magnitude of once every five years is why we excluded the patient.

Todd: One of the last people raised and I know we are about to run out of time here, if we are not a little bit over, asked the question about outliers. In VA when you are using activity based costing data like the managerial cost accounting data systems, there are two types of outliers. I want to be very careful about how people think of outliers. Usually we use the term outliers just to mean an extreme value but often people implicit and we mean an extreme value that is erroneous. There are both very high cost patients that are truly high cost patients, the patient who spends three hundred days in the ICU. That is a very large cost that is going to change your modeling approach to how you look at the statistical data here but it would be a true cost estimate or relatively accurate true cost estimate. Be careful when you use the term outliers. When we think of errors in data you can have both low cost errors and high cost errors and they both affect kurtosis, they both affect the modeling implications so you need to be thinking about true accuracy at both the low and the high cost not just this question of – is there an outlier here.

Dr. Ciaran Phibbs: Yes.

Todd: I think we are way over our time, but I appreciate people hanging on. It looks like we have gone through all the questions, if any other questions come in we will get back to you Ciaran and get back to them. So thank you very much for…

Dr. Ciaran Phibbs: Yes you can send those email.

Todd: Alright. Heidi can we turn it back to you to close.

Heidi: You certainly can. If you do have any outstanding questions that did not get answered you can send those into: HERC@va.gov and they can get those forwarded on there. We do as Ciaran was saying, we have our next session in the series two weeks from today I know most of you are registered for it I will be sending additional registration information out in about a week, we hope you all can join us for that.

When I close the meeting out in just a moment you will be prompted with a feedback form, please take a few moments to fill that out. Your comments there will help guide the rest of this series so if you have any changes or anything you could like to see we can definitely get those passed along to HERC.

Thank you everyone for joining us for today’s HSR&D Cyberseminar and we look forward to seeing you at a future session. Thank you.

Dr. Ciaran Phibbs: Thank you.