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Session: New Recommendations for the Conduct of Cost-Effectiveness Analysis from the Second Panel on Cost-Effectiveness Analysis in Health and Medicine

Presenter: Douglas Owens, MD, MS

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Dr. Paul Barnett: Hi, this is Paul Barnett from the Health Economics Resource Center. It’s my distinct pleasure to introduce today’s speaker, Doug Owens. Doug is a internist in the VA Palo Alto Health Care System and he’s Associate Director of our COIN Center here. You may know his name because he has been awarded the VA Under Secretary Award for Outstanding Achievement in Health Services Research. Doug is also the Henry J. Keyser professor at Stanford where he directs a couple of centers including the Center for Health Policy and the Center for Primary Care and Outcomes Research.

But I think most significantly today is that Doug is fighting the good fight in terms of evaluating the value of healthcare interventions, in terms of his research but also on numerous panels that he’s served on and setting guidelines and developing the recommendations for what we should do in U.S. healthcare that are value based. He is currently a member of the U.S. Preventive Services Task Force which develops the national guidelines that define preventive services for your health plan, at least as long as the affordable care act is still in effect. And you know I could go on and on because he is involved in so many different panels and programs and things like that but most significantly today in prevent the Public Health Service panel that defines how we should be doing cost-effectiveness analysis. So my great pleasure to introduce Doug.

Dr. Douglas Owens: Paul, Thank you so very much for the very kind introduction and I’m delighted to be invited to talk to you all. So as Paul mentioned, I was on the 2nd panel on Cost Effectiveness in Health and Medicine and what we’re going to do today is sort of an overview, a kind of a high-level overview of some of the recommendations and I’m going to talk about ones that I think are different and potentially important. And at the end I believe that we will have time for questions about this, so I look forward to discussing your questions at the end so I’ll get started here.

Those of you that have done cost-effectiveness analysis, you may know about the original panel. The Gold Book which was published in 1996. The first book was, the first panel was an attempt to help define best practices or to recommend best practices for the conduct of cost-effectiveness analyses as many of you probably remember or know. They made recommendations for a reference case analysis. The idea behind a reference case analysis was to set out recommendations about how to conduct specific analyses that would be comparable between different studies.

So the idea behind the reference case is to help provide some comparability. One of the issues at the time was that cost-effectiveness analyses were being done in various ways, meaning it was hard to take one study and compare it to another. Another important aspect that came out of the first panel was the emphasis on using cost per quality adjusted life years or QALYs as I’ll call them during the call. And we’ll talk a bit more about that in our new recommendations.

This book was widely used for cost-effectiveness analysis but because it had been so long, a new panel was developed with the idea that this could use some updating. And I want to first acknowledge both for this talk and for the work that I’m going to talk about, the 2nd panel. The co-chairs were Peter Neumann and Gillian Sanders from Duke and you see the list of people here that were decision scientists and health economists, clinicians, people that do evaluation of technology. The leadership group is down at the bottom, Peter and Gillian along with Ted Ganiats, Joanna Siegel and Loise Russell. They were involved, some of them were involved in the original panel.

And so again the idea was to do an update and I would also point out looking at the members in the panel that one of the things that we tried to do was get a bit more international input on this go-around. So David Feeny from McMaster, Murray Krahn from University of Toronto, Mark Sculpher from University of York, Mark is with the health economists in the U.K. who worked a lot with NICE. And so they helped provide an invaluable perspective on how these kinds of analyses are done and used in other places.

Here's the group. I’d like to say we were thinking great thoughts but we might have been trying to stay awake after lunch. And here are the places where the members came from. Funding for this 2nd panel came from several sources; RWJ, the Bill and Melinda Gates foundation, AHRQ and SMDM and our thanks to them for helping support this. It was about a five-year process. We had a number of meetings and in-person meetings and then innumerable conference calls so we’re grateful for the support. It wouldn’t have been possible to do it without that.

So I’m going to jump into the overview of the key recommendations but first let me ask and this will be a question you can answer on your screens. How many of you have been involved in or conducted a cost-effectiveness analysis? That will help me tailor the comments if I have a sense for how many of you have been involved in this at some level. And while we’re\_

Heidi: \_We’ve got that pole open. We’ve got that pole open, let’s just give everyone a few moments to respond and we’ll, and I’ll give you the results of that there, Doug. Responses are coming in quickly. It’s just a few more seconds and I’ll have that for you. Ok, so I’m going to close that out and what we’re seeing is that 66% of the audience saying they have not conducted a cost-effectiveness analysis and 34% of the audience saying that yes, they have conducted a cost-effectiveness analysis. Thank you everyone.

Dr. Douglas Owens: Fantastic. Thank you, Heidi. That was quick, okay, fantastic. Well so, many of you have a lot of experience with this and those of you who have not conducted a cost-effectiveness analysis, I hope that this will provide an overview of some of the main issues to contemplate in case you do. And let me start by posing two kinds of cost-effectiveness questions just, and I will refer back to these as examples during the presentation today.

But first, let’s think about implantable defibrillators. Implantable defibrillators are something that you put in to help prevent sudden cardiac death if someone is at risk for sudden cardiac death because of a particular heart condition. This is something that we’ve worked on for many years and I use that as an example because it’s a healthcare technology and because we will see, you know, really the effects of an implantable defibrillator are things that primarily affect health and it’s not an intervention that has broader consequences.

The second example would be treatment of opioid use disorder. So opioids, as you well know are a national public health emergency now. Many effective treatments. And suppose that you were going to do a cost-effectiveness of opioid use disorder. One of the things about that is that opioid use treatment has implications not just for the health care sector but also for the criminal justice sector or perhaps other sectors and so, in this situation you have a cost effectiveness analysis which has broader ramifications and broader consequences than just in the health care sector. And I’m going to refer back to these two examples as we go through some of these recommendations because in part the recommendations are intended to help people think through the issues as they’re designing and conducting a cost-effectiveness analysis and what the implications and consequences of an intervention are broadly. Maybe it’s just health related but maybe it’s broader than that. So without further ado, let’s just talk about some of these recommendations.

And the recommendations came out in two ways. There’s a book. This is the new book that you see on the right of your screen. There’s also a paper in September of JAMA which is, I think, a pretty concise overview of the recommendations so that would be a way to get into the recommendations without diving into the entire book. The book has, as I’ll explain to you, a number of chapters with a lot of detail and helps lay out the thinking behind some of these recommendations. So let me just explain what’s in the book.

The chapters are as follows; using [unintelligible 9:28] CEA, here’s a chapter on theoretical foundations, then reference cases, how to design a CEA, a chapter on modeling, estimating consequences and that’s health consequences, valuing health outcomes, thinking about costs, evidence synthesis, discounting, uncertainty analysis, ethical considerations and then how to report the cost-effectiveness analysis. A number of these are actually new which was indicated there. These are new chapters where we thought that the field had moved and evolved since the first book and that we needed to deal with some of these topics in substantially more detail than they had been in the original book.

So let me start with the reference case and impact inventory, and I’ll just say at the outset I think these may be some of the most important new changes in recommendations and as we go through these, I’ll just say at the outset that I think that these are intended to be useful guides. In many situations there may be other approaches that you would want to use. This is not meant to be absolutely prescriptive but to help people sort of, as they work through doing a cost-effectiveness analysis.

So in terms of the original panel’s recommendation, they recommended a reference case as I mentioned. The reference case was meant to provide comparability across different analyses. They recommended a societal perspective and the societal perspective [unintelligible 11:04] is that you would count all costs and all benefits no matter to whom they would accrue or occur and that you consider all the parties affected by an intervention and then address specific decision contexts as needed. The societal perspective in the reference case that was suggested in the original book may not be the most relevant or might not have been the most relevant analysis for the particular decision makers that you were working with or your intended audience. And so, other analyses were certainly expected that might be different than the societal perspective or different than the reference case to fit the needs of particular situations and decision makers. But these are the main recommendations that I think helped frame an approach to doing cost-effectiveness analysis with the intention of increasing methodological rigor and also transparency and the comparability of cost analyses.

Since the original panel there’s been a great deal more experience with cost-effectiveness analyses and Peter Neumann in particular, who has a registry of many of the cost-effectiveness analyses that have been done has analyzed this, and many CEAs, in fact probably most, don’t really use societal perspective and many claim to and I had to put myself in that category when they probably really didn’t in the sense that the societal perspective was outlined in the original guideline. And so some elements were often omitted from the societal perspective in many of the published analyses and decision makers who use cost-effectiveness analyses often have taken a more focused perspective than societal.

So we wanted to sort of recognize and acknowledge those issues. We recognize the appeal of the societal perspective. At the same time there are challenges associated with it. Is there really a single societal perspective? Here we got input again from our colleagues in the U.K. and Canada where really they have much different situations than we do in the U.S. where there are fixed budgets with budget constraints and they made the case very clearly that the societal perspective might differ in different contexts. At the same time, we did agree with the first panel on the need to promote quality in terms of the methodological approaches and comparability to the extent possible. So that was part of the motivation behind the recommendations that we’ll talk about.

And in particular, here’s the recommendation about reference cases, and this is new and different than the original panel. We suggest that all studies represent a reference case analysis based on a health sector perspective and a reference case based on a societal perspective. The reason for that is as I mentioned that many analyses that have been published really didn’t use and perhaps they had good reasons not to use societal perspective. We’ll talk about when these are different, but we recognize that societal perspective might not be appropriate or might not be feasible even though it’s desirable in many cases. And so this recommendation is to use two different reference case analyses. We continue to recommend that the health effects be measured in quality adjusted life years or QALYs and again our hope was that these recommendations would enhance consistency and comparability. And we’ll come back to sort of what the differences are in the health sector perspective and the societal perspective in just a moment.

The health, in the health sector perspective we recommended that results should be summarized with incremental cost-effectiveness ratio. Net monetary benefit or net health benefit might be also reported and that people should consider a range of cost-effectiveness thresholds. Of course in the U.S. we don’t really have a particular cost-effectiveness threshold. That’s different, to some extent, in other countries. But the idea here is to allow readers to understand the implications of the value of a healthcare intervention across different cost-effectiveness thresholds where perhaps beauty is in the eye of the beholder what your threshold should be may differ between different users and readers of these.

The second major I think difference or new recommendation in the new panel is the recommendation to use an impact inventory and I’m going to explain what that is and go through it in some detail. The idea is to include an impact inventory table which lists the health and the non-health impacts of an intervention. The purpose is really to ensure that all the consequences of an intervention, including those outside the formal health care sector, are considered in a systematic and comprehensive way. We hoped that this would provide a framework for organizing and thinking about and presenting various types of consequences. And so I’m going to go through now the healthcare, the impact inventory and hopefully explain what we meant by that.

So here’s the idea of an example of the impact inventory. If you take a look, the columns of the impact inventory show the health sector or the sector of the formal health care sector at the top, an informal health care sector at the bottom that would be patient, or in the middle, that would be patient time costs, unpaid caregiver time costs, transportation costs. And then non-health care sectors and these are examples, so productivity, consumption, social services, legal or criminal justice implications, education, housing, environment, etc. And if you look in the second column, here we have the types of impacts. So this is meant to be, you know, what are the consequences in these sectors. So for example, in health, the health outcome effect at the top in the second column, the effects of mortality, so that would be longevity effects. Effects on quality of life and then other health effects, adverse events, secondary transmission of infections, etc. depending on the kind of analysis that you would be doing.

The medical costs would be cost paid for by third-party payers, paid for by patient’s out-of-pocket, future related medical costs and future unrelated medical costs. So in this recommendation we are suggesting that in the healthcare perspective that the costs that you include encompass all of the ones hear that are listed including, which one area that some people may not have been doing in the past, future related medical and unrelated medical costs. So that would be for example the cost of someone’s healthcare over time and if you have an intervention that prolongs life, it means that people will also be consuming healthcare longer and those costs would be included.

In the informal health care sector, the costs would be patient time costs, unpaid caregiver time costs, transportation costs. How important those are will of course depend on the specific problem that you are evaluating and these are included in the societal perspective but not in the healthcare perspective. And then the non-health care sector impacts below are also included in the societal perspective but not the healthcare perspective and those include productivity, so labor market earnings lost, the cost of unpaid lost productivity due to illness, the cost of uncompensated household production, consumption [unintelligible 19:24] to future consumption unrelated to health, social services that might be included as an intervention, legal or criminal justice issues, education, housing, environment, etc. and there are examples there listed.

So now two points that I want to make here are that you can see from this what is included in the healthcare perspective and what’s included in the societal perspective in these next columns. And the idea behind impact inventory is that you can denote what is included in the analysis both in the health care sector perspective or other perspectives. Sorry about the background noise here. And that you can identify for readers in this list, essentially around the checklist whether or not you included these different items. So if you had an analysis where you are only doing a health care sector perspective, you would have the second row there included. If you were doing a societal perspective, you would have a more extensive list, and then a reason for why you included or didn’t include a particular item in the impact inventory and in the analysis and then there’s notes to sort of explain the rationale behind it.

So now let’s think about the consequences again. So the sections of the impact inventory divide the consequences as I’ve mentioned into different sectors. So here’s the formal health care sector, here’s the informal health care sector in this row and then the non-health care sectors. So for each type of impact, the specific effect or cost, the checkbox indicates whether it’s included in the reference case analysis from a particular perspective. And again, the idea here is to give the readers sort of a guidebook about what’s in your analysis and what’s not. So for example, in an analysis you would of course usually include longevity effects, health-related quality-of-life effects and other health effects. And those would go in both the societal and the health care sector perspectives.

For informal health care sector, those would not be included in the health care sector analysis but would be included in the societal perspective. Again, the importance of these depends on the specific problem that you are evaluating. And then the non-health care sectors that are shown here and you might, for example, include some but not others and the impact inventory gives you a way for noting that for readers to understand what’s in and what’s out of the analysis. You may have good reasons for including or not including something but the idea is this helps with transparency and helps the readers to understand what has been included in the analysis.

So to summarize, the main purpose of the impact inventory is to ensure that all the consequences including those outside the formal health care sector are considered routinely and comprehensively and we hope it will provide a framework for organizing, thinking about and presenting various types of consequences.

So let me go back now for a minute to the two examples that I opened with and I’m going to go back to the impact inventory here. And think about implantable defibrillators, for example. These are devices you put in to\_

Dr. Paul Barnett: [unintelligible crosstalk 23:40] \_before you take that up, I just wondered if you might reinforce what we mean by a reference case analysis because there was a question by that and I want to make sure that people are clear about that.

Doug Owens: Absolutely. A very good question. So the reference case analysis is meant to be an analysis that uses, that conforms to the recommendations that are outlined in the book and those recommendations will be about what’s in the analysis, what’s included. That’s what we’re going through here on the impact inventory, what’s not included, what discount rate you use, etc. So again, the reference case is meant to be sort of the guidelines about what should go in and what methods you should use. And the idea behind the reference case is that if I did an analysis of defibrillators and you do an analysis of breast cancer screening, if we both do a reference case then the methods of those analyses will be similar enough that it is useful for or we have the ability to compare between analyses. And that’s the idea behind the reference case. The health sector reference case includes a more limited set of outcomes that are related only to health as we were talking about here whereas a societal reference case would include not only health care sector, formal health care sector but also informal health care sector and non-health care sector consequences. So Paul, does that help?

Dr. Paul Barnett: \_absolutely that’s great.

Dr. Douglas Owens: Ok, good, good and I’m sorry that wasn’t clear. So let me think now, we’ll go back then, I’d ask you to think about the two analyses that, or problems that I posed at the beginning was one is the implantable defibrillator and the second is treatment of opioid use disorder. I think what you would see here in thinking about those is that the implantable defibrillator in the health care sector perspective would encompass really probably all the consequences you’d be worried about. Their health. It doesn’t really have, it might not include patient time costs or unpaid caregiver time costs or transportation costs possibly, but the main impact of a technology like implantable defibrillators is in the health care sector. And so the difference between a health care sector and societal sector analysis might be very, there might be very few differences between those.

On the other hand, if you think about the problem of opioid use disorder treatment, for example, there are of course clearly implications for the formal and informal health care sector. But there are also substantial implications at least for legal and criminal justice and possibly for productivity and social services and maybe others as well. And there are estimates in the literature for example for opioid use disorder treatment that the savings from successful treatment are larger in the criminal justice system than they are in the healthcare system. I’m not saying that’s true but my point is that there are some interventions for which these non-health sector consequences are very, very important. And the idea here is that this would, the impact inventory gives you a way for thinking about those issues as you design and conduct your analysis and for communicating those issues to the reader. What did I put in, what did I not? And for example, if you were doing a cost-effectiveness analysis of opioid use disorder and you decided for whatever reason that you did not want to include the non-health care sector, someone could look at the impact inventory and they could understand that that’s not in the analysis and you’d give a rationale for why you chose not to do that.

So those two examples, I think, help understand how the impact inventory might be used and how the differences might play out in terms of the perspectives that you use, healthcare versus societal and where there may be important differences. So for some interventions, the difference, there might be quite a substantial difference between the health care sector perspective and a societal perspective. Of the other interventions, those might be almost identical analyses.

All right so I’ll continue on now talking about the impact inventory and the reference case analysis. Again, with the impact inventory purpose to ensure that all the consequences in both health care and non-health care are considered and that the reader can understand what you’ve included and what you haven’t, and providing a framework for thinking about that. Quantifying and valuing non-healthcare components in the impact inventory, I’m not going to go into this in great detail other than to say that our recommendation is that analysts should attempt to quantify and value non-health consequences unless those consequences are not likely to have a negligible effect on the results of the analysis.

So for implantable defibrillators, there’s really not an issue apart from possible informal health care sector, the other sectors aren’t really likely to be important and you would just say that, say we didn’t think that was important for this problem. For opioid use disorder treatment, these non-health sector effects and consequences cost and effects would be potentially quite important and so our recommendation is that you attempt to quantify and value those if you decide that’s out of the scope of the project that you’re trying to do or you can’t do, or don’t have the resources, then you would just explain that and the rationale for not doing that and then the readers could be aware of the fact that that part, the non-health care sector effects are not in the analysis as something for them to contemplate.

In terms of whether you report or when you report incremental cost effectiveness ratios, we of course acknowledge in this first bullet point it would be helpful to inform decision makers through quantification and value of all health and non-health effects of intervention. However, in terms of non-health interventions, there are really no widely agreed on methods for quantifying and valuing some of the broader effects in a cost-effectiveness analysis which may mean that it is challenging or not feasible to report on incremental cost effectiveness ratio.

So we suggest that analysts present the items listed in the impact inventory in the form of disaggregated consequences across different sectors and then use one or more summary measures such as the incremental cost effectiveness ratio, net monetary benefit or net health benefit that includes certainly the items in the health sector perspective. And then identify which items are included and how they’re measured and valued. And the reason that we landed on this recommendation is the challenges associated if you really have something that has non-health sector costs or benefits.

How would you summarize that in an incremental cost-effectiveness ratio or maybe the thresholds for cost effectiveness in different sectors or different, etc.? So we felt that it was, in some situations the better part about it might be just to report these disaggregated costs and consequences but that using an incremental cost-effectiveness ratio or another summary measure for the healthcare perspective would make sense. So that’s the set of our recommendations around the reference case, the impact inventory and how to report those things. So at this point, I’m going to move on\_

Paul Barnett: \_Doug we had a question about some acronyms that were on page 16 and it just occurs to me that a lot of these, if you go back to that prior slide for just a second which you had listed incremental cost effectiveness, oh you’re going to go back to slide 16. I was just saying all of those acronyms are written out on that slide. ICER, incremental cost-effectiveness ratio, NMB which is net monetary benefit, NHB, net health benefit and CE, cost effectiveness. So\_

Dr. Douglas Owens: \_Great, thank you, Paul\_

Dr. Paul Barnett: \_Just ah, we get so used to acronyms we forget that we’re using them.

Dr. Douglas Owens: Yes, with my apologies. I mean the one that most of you will be more familiar with is incremental cost-effectiveness ratio which is a way, which is sort of the most common way to summarize the results of cost-effectiveness analysis. Net monetary benefit, net health benefit are simply ways of converting that into, for specific cost-effective thresholds and to other summary measures, but for most intents and purposes people are reporting incremental cost-effectiveness ratio and Paul, I don’t know if you’d like to add something else on there.

Dr. Paul Barnett: Nope, I just wanted to, there’s the key thing, I just thought oh, they were asking questions about those and there they are, those acronyms spelled out so I just wanted to point, make sure we pointed that out to them.

Dr. Douglas Owens: Great, thank you so much. And so I’m now going to move on to valuing costs and I’ve talked about this, I’m not going to go into a lot more detail. We’ve talked about it some when we looked at the impact inventory. The societal reference case would include medical costs both current and future related to the disease and unrelated to the disease, borne by third-party payers and paid for out-of-pockets. It would also include the time costs of patients who are seeking and receiving care, the time costs of informal unpaid care givers, transportation costs, effects on future productivity and consumption and other costs and effects outside the health care sector.

As you can see that’s some, in some respects, an ambitious proposal in terms of what kind of costs that you would include. I think the things that we’re maybe more used to including would be the medical costs, time costs, informal unpaid caregivers time costs and transportation potentially. And again, whether these are important or material to an analysis depends on the kind of analysis that you are doing. And so for example, if you’re looking at the cost effectiveness of interventions for dementia, the time costs of informal unpaid caregivers, family members, might be a very important component of that. But for implantable defibrillators, probably is not unless there are special circumstances. So the relative importance of these depend on the kind of problem that you’re doing and in the impact inventory you can indicate what you’ve included what you haven’t and why if you think that something is unimportant, you can say that.

Let me move to valuing health outcomes now and our recommendation is that health consequences should be aggregated into a single measure using quality adjusted life years or QALYs and that you use community-based preferences and I’ll talk a bit more about that. And for the reference case, we recommended the use of generic preference-based measures. Things like the EQ-5D. We did not recommend a particular measure. And let me first talk about the rationale for QALYs. A QALY, for those of you who aren’t familiar with that, is a measure that encompasses both the effects on length of life and the effects on quality of life. And so it’s very appealing in the sense that you can capture the important consequences of, some interventions might increase of life and increase quality of life but some interventions might not have an effect on either length of life of quality of life and some interventions might have opposite effects. It might increase length of life but decrease quality of life. Think of chemotherapy for example or something like that.

So using QALYs allows you to assess comprehensively both length of life and quality of life and that’s important. I’m not going to spend a whole lot of time given where we are in terms of time on community preferences. The idea behind community preferences that would be using measures that have assessed the community members about the quality of life of different interventions is that if you’re allocating public resources, that the public views of the quality of life associated with certain conditions should be incorporated. I would just say that we recognize there will be circumstances in which community preferences may not make so much sense or may not be available. Patient-based preferences or utilities might be reasonable to include in an analysis and again, I guess our thinking was include, describe transparently what you included, why you included it. And in situations where there are both community preferences and patient based preferences, at least my own personal practice is that I would use both to see if they mattered and if they do matter, we’d talk about that or let the readers know about that.

I’m going to skip this slide because it really has some of those issues that I just talked about. Just to illustrate if you aren’t familiar with QALYs, this is just a graphic on it. Here quality of life is on the Y-axis from 0-1 and these are different dates, month one and year two and month one and year four, so different durations. And so you calculate QALYs, if you were just adding up life years, you’d have this first interval in blue which is two years and the purplish one is one and a half and one year then two and a half and so that’s seven years. But a quality adjusted life year you multiply the quality times the length of time you spend in that health state and so that would be calculated in this way by multiplying the quality of life times the duration for each of these intervals and that would be 5.6 quality-adjusted life years.

The rationale for that is that you know, both quality of life and length of life vary and that this is life path of health-related quality of life over years. Quality of life again 0-1 on the Y-axis. The QALYs are the area under that curve. And then if you have a treatment that might affect both length of life and quality of life, the incremental QALYs would be the difference in the areas under these two curves and again, it allows you to capture effects of both length of life and quality of life.

So I’m going to leave that now and talk about conducting and implementing CEAs and just hit a few issues that came up in the recommendations. The first on which I think, which is new and is that we recommended using a written, publicly available protocol. As you well know probably for clinical trials, it’s the standard of practice so to speak. Trials have to be registered if they’re going to be published and we felt it would be useful to move in that direction to the extent that you specify ahead of time the objectives and the type of analysis, your perspective interventions and comparators, the population, the time horizon, the sources data assumptions and analysis plan and make that available to people. If you amend that as you go, which is almost always the case, then you would update this protocol appropriately. But the idea here is to let the readers and the public know what your intention is and in a way that’s specific so that people can judge whether you’ve then approached the analysis as you intended to or as you said you were.

There is work going on new on whether models should be shared, etc. We did not get into that in the 2ndpanel. Let me make the comment about decision models and the view of the 2nd panel is that decision models would usually if not almost always be needed to do cost-effectiveness analysis. They’re needed for extrapolation in several ways. One is potentially beyond the time horizon of the available data. Another might be from intermediate or surrogate outcomes to long-term outcomes to population subgroups not observed in studies. When long-term outcomes associated with diagnostic test strategies might not be laid out you may have to model that. And then potentially strategies that have not been studied in head-to-head comparisons.

And one of the points I’d make related to this which I think many of you are likely aware of is that time horizon is especially important and a recommendation related to time horizon of a cost-effectiveness analysis is that it should be long enough to capture all of the consequences of the intervention. That is all of the benefits and all of the costs and for many interventions, that’s life-long, so treatment of HIV, putting in an implantable defibrillator, treatment of opioid use disorder. All of those interventions would have consequences that extend potentially over the entire lifetime of the person who receives them. Incremental cost-effectiveness ratios vary by time horizon. This is an analysis which looked at the cost-effectiveness analysis of I believe this is the implantable defibrillators based on time and you get very different answers based on different timelines and the mistake that people can make that we are worried about is using timelines that don’t capture all the consequences.

So modeling is going to mostly be used, needed in these situations and we had a few modelling recommendations that will be familiar to you for those who do this. The conceptualization of the model should be independent of the data identification phase. In other words, you don’t just model what you have data for, you have to think about the model independently to that. You should document and justify the structural assumptions that you make in a model. The analyst should specify the starting population whether they’re analyzing a cohort or a population and validation of the model should occur throughout the conduct of the CEA and that should be made available to readers.

I’m going to leave modeling now and talk briefly about uncertainty analysis. So there’s a chapter on uncertainty analysis which goes into a great deal of detail. Some of the highlights are the propagation of the input uncertainty informs entire decision uncertainty. People should consider correlations among parameters when that’s possible to do. Structural uncertainties should be explored in scenario analyses and expected value of information, I’m sorry for that acronym, that stands for expected value of information, should be used to guide decision making under uncertainty. Those of you familiar with that, it’s an approach for identifying how much additional information, how useful additional information can be. I’m not going to talk about it in any further detail but it’s explained in the book.

In terms of structural uncertainty, the topic means how to model some intervention beyond the time horizon of data. How do you structure your model? How do different states of health and pathways get characterized in a model? How does disease progression, how is it modeled over time? And the judgments about the relevance and appropriateness of different sources of evidence.

In terms of sensitivity analyses which most of you will be familiar with, that’s part of uncertainty analysis, it’s not the only part of uncertainty analysis. This involves examining model outputs while conditioning on specific inputs to provide insight both about the model behavior in one and multi-way sensitivity analyses and threshold analyses. These are often, they’re almost always a very crucial part of an analysis. They might in fact be the most important part in some analyses depending on the kind of uncertainty you have. And they can also be used as a means of understanding the implications of heterogeneity both in treatment effects or in population heterogeneity and so it can be very, very useful. I like to characterize these as understanding the importance of your ignorance in terms of what you don’t know about the problem and sometimes that’s the most valuable insight to come out of a cost-effectiveness analysis.

This next section is on reporting CEAs and I’m not going to dwell on it because I do want to leave some time for questions but I’ll go through it briefly and then that will sort of wrap up the presentation and then if there are further questions be happy to talk, to discuss those.

The recommendations on reporting really is the purpose is to increase the transparency completeness and comparability of reporting. One of the main issues from the point of view of decision makers about cost-effectiveness analyses, particularly ones that are based on complex decision models is how they understand what’s been done. And how do you convey to the readers and to the users of a cost-effectiveness analyses, what are the crucial assumptions? What are the important uncertainties? And so in reporting, we hope to provide some help about how to do that. And there are updates about using structured abstract, the impact inventory, intermediate outcomes and disaggregated results and again, I’m not going to dwell on them. You can see these slides and it’s in the book. But a structured abstract includes some of these, you might not include them all. Elements in the format are listed here.

There’s also a reporting checklist that we hope will be useful to people as they’re reporting analyses which is fairly long but you can use it both for your own purposes and we don’t know whether people want to publish that. But in summary, the idea is to increase the emphasis on transparency and enough detail should be provided to allow for replication when possible. So in a structured abstract with a checklist, the impact inventory, intermediate outcomes and disaggregated results and a technical appendix. And for those of you have conducted cost-effectiveness analyses, you’ll know that many journals want many of these items and so we’ve tried to formalize that in some way. We of course think that issues of conflict of interest should be presented in a transparent way.

As I mentioned, there’s work now on sharing models and making models public. There was recently a conference on this. We did not tackle this problem. It’s a complex problem both in terms of intellectual property and in how people [unintelligible 47:28] will people actually be able to use your model if you made it public. I’ve said personally in our own experience, we have sometimes done this, made the models publicly available or available to people who ask. I think how useful this is is yet to be determined but I think there is a push for the underpinnings of our work to be able to be evaluated very carefully by other parties.

So let me summarize. I think the key changes really are the recommendation to do two reference cases. The health care sector which really includes consequences and costs in a formal health care sector and the societal perspective which is much broader and includes the informal health care sector as well as non-health care sectors. The impact inventory is a way of organizing and presenting to people what you’ve done and what’s in your analysis and what’s out of your analysis. And really it’s a way both to organize thinking about the analysis and to improve communication about it. So Paul, with that, that’s the end of my formal remarks and if there are questions that we can work through that, I’d be delighted.

Dr. Paul Barnett: Yea, so someone, Teryl Knuckles wrote I am familiar with posting systematic reviews on PROSPERO. Where can cost-effectiveness analysis protocols be publicly posted.

Dr. Douglas Owens: Well that’s a great question. And we, you know, I’m not aware. That’s one of the issues that people would have to, that needs to be tackled. I should have mentioned, we are writing a follow-up piece on this on sort of future research questions and priorities. And with respect to protocols, I think that’s really a very important one. Right now there is no mechanism that I’m aware of that you can put these. I guess in the meantime, my own thought with this would be just to make it public just to note that it is available but that’s a key step and I don’t think we’re quite there yet.

Dr. Paul Barnett: Well I guess one can always, many journals now have online ways to publish stuff. That is you can have supporting documents. But it is, if you want to do it apriori that’s not possible unless you say date it somehow. I had an interesting question I’ll raise is we did a cost-effectiveness analysis on a VA cooperative study of smoking cessation integrated with Post-Traumatic Stress Disorder care and the interesting thing is when we ran the analysis and we just looked at the smoking cessation services cost, we found that it was a cost-effectiveness use of healthcare resources. But when we added in all of the costs of healthcare of our cohort, there was so much variance, lots of noise, that the cost effect, it was no longer cost effective because the costs became you know, wildly noisy. And so it was only when we excluded those other healthcare system costs. So there was no significant difference between the treatment groups of those other costs. And I’m just asking, is there an unintended consequence of adding in all of these other, perhaps unrelated costs, into our cost-effectiveness analysis that it becomes more difficult to detect significance in cost-effectiveness.

Dr. Douglas Owens: That’s a very good question, Paul. Let me kind of explain, at least my view of the rationale behind that of why you would include other healthcare costs. Let’s take an example of HIV screening for example where if you screen someone, you identify them, you treat them and they may live 20 or 30 years longer than they otherwise would live without treatment, you know, the numbers are different but take that as a hypothetical. If you don’t count the additional costs of healthcare while they’re living longer, 20 or 30 years, you could make the argument that you’re underestimating the actual economic costs that are going to accrue because of that intervention. Of course people are living longer also and so you get that on the benefit side. So that’s part of the reason.

I think the challenge that you’ve pointed to is that sometimes it’s not as easy to do that as you would hope and so I guess as my thought would be like in a situation that you, that you identified, that you’d be transparent and explain that to the readers about what the issues were and as you did analyze, you could analyze it both ways and see what the impact was and explain the circumstances. I do think it is a problem to ignore other costs when an intervention is going to end up resulting in costs, just leaving those out of the analysis I think can be problematic but part of the impact inventory of course is to make it clear to people what you’re putting in and what you’re not putting in and in situations like you described, maybe you do it both ways and be transparent about what the issues are.

Dr. Paul Barnett: Yea, that worked for us, the referees accepted that so\_

Dr. Douglas Owens: \_Okay\_

Dr. Paul Barnett: \_ interesting. So we have another question. Please explain reference case analysis again, so that seems to be a popular question.

Dr. Douglas Owens: Okay, so and I’m sorry that that’s not clear but ideally the reference case, let’s say that we’re doing implantable defibrillators and the reference case for that from a healthcare perspective. So what we recommend that goes in the reference case is the health consequences and the costs, which costs go in it? We have recommendations, I didn’t go over these. We have recommendations about the discount rate that you use, further recommendations about how you identify and quantify costs. And so the reference case is an analysis that you conduct that uses, that adheres to these recommendations about what’s in and what’s out, how you value the health outcomes, how you count the costs, what discount rate do you use for costs and health benefits, etc.

And so the idea is that if I do a reference case analysis on implantable defibrillators and Paul does one on smoking cessation, we’ve used similar methods and so when he gets an incremental cost-effectiveness ratio for smoking cessation, I get one for implantable defibrillators and because we’ve used similar methods about how we count the consequences and how we count the costs and how we discount the costs and benefits, etc., those analyses will be more comparable and so making a comparison between the two studies is more legitimate or is more likely to give you a reasonable inference. So that’s the idea behind the reference case is that it’s a case that’s done according to these recommendations in the book for comparability.

The health care sector reference case simply includes just the things in the formal health care sector that we talked about on the impact inventory whereas a societal reference case is a much broader analysis. It includes both healthcare, formal health care sector, informal health care sector and non-health sector costs like criminal justice costs, etc. Obviously those could be, it can be ambitious to do those for some problems But that’s the idea that, if, you know my reference case for breast cancer screening has used the same methods as Paul’s reference case for Hepatitis C treatment and so when we get to incremental cost-effectiveness ratios, we have a sense that maybe those can get us a comparison that’s informative. As opposed to\_

Dr. Paul Barnett: \_Even two studies of implantable defibrillators, right?

Dr. Douglas Owens: Absolutely\_

Dr. Paul Barnett: \_You know compare Doug’s study to Gillian’s study to make sure, and maybe they have different results but you want to make sure it’s not because of the methods you chose.

Dr. Douglas Owens: Absolutely. And the sort of the counter factual is that Paul uses, you know, he put some kind of costs in that I don’t put in and he uses a different discount rate than I do and he counts his, used a different approach to evaluate health outcomes, our analyses come up with very different answers and we don’t know if it’s because of the methods or it’s really a difference in the value of the intervention.

Dr. Paul Barnett: So somebody, McKalia [phonetic], I’m not going to be able to pronounce her name, wrote so is the reference case basically the format in which you will analyze your case?

Dr. Douglas Owens: Well the reference case. So that’s a good question and the reference case is one case that you would present. You’d say, here’s our results. Here’s the cost effectiveness of implantable defibrillators or Hepatitis C treatment for our reference-case analysis. And for our healthcare, let’s say our healthcare perspective reference case. And then you would have an impact inventory that shows what you put in the reference case analysis and what you left out of it. You might then, depending on the purpose of your analysis say, well you know, our healthcare plan is really interested in this but they have a different perspective. I’m going to use a different perspective than the health sector perspective which really is more focused on our health plan. You could report that analysis, too. We’re not saying that the reference case is the only thing that you should report. The idea though is that if you report the reference case along with whatever other analyses you’ve constructed however you want to do them which may be relevant to your decision makers or purpose. But if you’ve reported the reference case then that allows me to compare my study to Paul’s study to Gillian’s study etc.

Dr. Paul Barnett: It’s a template or set of methods\_

Dr. Douglas Owens: \_It’s a set of methods, that’s right.

Dr. Paul Barnett: Right, right. Well, you know we’re very close to the top of the hour and we don’t have any other questions so that’s a golden coincidence so maybe we ought to thank you, Doug, for your presentation and invite people to take the, Molly, you’re going to give us a poll, right?

Heidi: No this is Heidi and we already put the poll up.

Dr. Paul Barnett: Oh, Heidi\_

Heidi: \_no that’s fine. We completed that at the beginning of the session\_

Dr. Paul Barnett: [unintelligible crosstalk 58:44] the feedback\_

Heidi: \_Oh the feedback form. Yes. So what is going to happen to the audience. If you could all just hold on. When I close the meeting out, you are going to be prompted with a feedback form. Please take a few moments to fill that out. We really do appreciate your feedback and I believe that HERC uses that for their annual report. We really do count on getting good solid feedback from all of you and really want you to plan our upcoming session. Our next session in this course is scheduled for next Wednesday. Risha Gidwani-Marszowski will be presenting An Overview of Decision Analysis. Registration information was sent out a few hours ago. Check your email, it should be in there if you are not already registered. Thank you everyone for joining us today and we look forward to seeing you at a future HSR&D Cyberseminar. Thank you everyone.

[ END OF AUDIO ]