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Introduction to Pharmacoeconomics  (SLIDE 2)

Welcome to the Introduction to Pharmacoeconomics module for the ISPOR Distance Learning Program.

Learning Objectives  (SLIDE 3)

There are several learning objectives associated with this module. By the end of the Introduction to Pharmacoeconomics module you will be able to: state the role of pharmacoeconomics in medical decision making; define the types of pharmacoeconomic cost-effectiveness analyses; explain the societal, patient and payer tradeoffs involved in using pharmacoeconomics for medical decision making.

Learning Objectives (cont’d)  (SLIDE 4)

You will also be able to understand the difference between and usefulness of average and incremental, also known as margin cost-effectiveness analyses; state the definition of utility measurement and its use in cost utility analyses; and understand the elements essential to a published cost-effectiveness analyses.
Introduction  (SLIDE 5)

We will be interested in pharmacoeconomic or cost-effectiveness analyses. Following are questions that we wrestle with in our health care systems: Can the health system support the additional cost for each life saved if the new drug is both more costly and more effective than previous therapies? If a new drug or device is less costly but less effective than existing therapies, how much of a diminution in efficacy can society, payers, and patients withstand in order to save money? How much money must be saved in order to make it cost-effective to accept a reduction in efficacy over existing strategies?

Use of Pharmacoeconomics / Cost-Effectiveness Analyses  (SLIDE 6)

Cost-effectiveness analyses first came of interest in the 1970s and have assumed greater importance through the development of more sophisticated analytic techniques because of the increasing prominence of these analyses in worldwide drug registration, formulary decision making, therapeutic guideline determination, and individual patient decisions. It is incumbent upon researchers and decision-makers to understand the basic tenants of pharmacoeconomic or cost-effectiveness analyses and how these may be applicable to health care systems and medical decision making.

Benefits from PE Analysis of Health Care Programs  (SLIDE 7)

There are multiple benefits that can be derived from pharmacoeconomic analyses and outcomes assessment. These include, intangible benefits (the value of health per se to individual consumer), the avoidance of future health costs, increased productive output due to improved health status and the use of evidence-based medicine to make the best choices for the population and individual consumers.

Outcomes Assessment and Pharmacoeconomics  (SLIDE 8)

Pharmacoeconomic analyses or cost-effectiveness analyses are used for outcomes assessment to determine the end result of the use of health care technology in cases where there are finite societal resources that require consideration of opportunity cost. Opportunity costs are the value of alternative uses of those resources. So for example, an opportunity cost might be what would be the cost of attending this lecture versus watching a show on TV – what would you get more out of? Depends what the show is I suppose. Health care reform has required methods to evaluate economic and societal value of goods and services and therefore, pharmacoeconomics is used to evaluate value for money expended on health care technologies.

Objectives of Pharmacoeconomics  (SLIDE 9)

The objectives of pharmacoeconomics are to apply economic principles to drug therapy interventions – that is, to prevention and/or cure associated with these different interventions; to conduct research that identifies, measures, and compares the costs, that is, the resources consumed; and the consequences of pharmaceutical products and services. This research is meant to improve individual and public health outcomes in addition to providing for more rational decision making, in terms of formulary management, medication choice, and system resource allocation.

Steps in Evaluating Type of Analysis  (SLIDE 10)
To evaluate health care technologies, we first have to determine what type of analysis will be performed. To do this we have to determine the efficacy or effectiveness of the therapies or health care technologies to be evaluated. Efficacy is that which occurs under optimal circumstances, such as during a randomized controlled trial. In contrast, effectiveness of a therapy is that which occurs under usual used circumstances once a drug or device is in the public domain and in general use. A further concept is that of efficiency which incorporates elements of cost into the picture. A Cost-effectiveness analysis or CEA is a comparison with an alternative therapy or therapies that requires consideration of costs, as well as specification of perspective, timeframe, effectiveness metric or measure, discount rate and assumptions. Varies disease endpoints that are affected by therapy such as risk markers, disease severity, and death can be assessed by corresponding indices of therapeutic outcome such as millimeters of mercury in blood pressure reduction, hospitalizations averted and life years saved, respectively.

Questions (SLIDE 11)

The questions we are evaluating in a cost-effectiveness or pharmacoeconomic analysis include: is the treatment effective? What will it cost? How do the gains compare with the costs? Typically, one chooses the option with the least cost per unit of measure gained. This is represented by the ratio of the cost to the effectiveness shown here as “C” colon “E” and is called a cost-effectiveness analysis.

Types of Pharmacoeconomic Analysis (SLIDE 12)

There are different types of pharmacoeconomic analyses based primarily on the unit of effectiveness. Cost-minimization analysis is used to assess therapies that have equivalent outcomes. So in effect, the denominator is inconsequential or not present. An example of use of this type of analysis is with equal potent antihypertensive agents. This type of analysis may be presented as a cost-consequence representation in which cost factors are presented individually rather than aggregated. Cost-benefit analysis measures benefit in monetary units. CBA may be thought of as the yield of an investment. There are three general approaches to the monetary evaluation of health outcomes: human capital, revealed preferences and willingness-to-pay. The human capital approach for example, measures the value of an individual’s contribution to society via his or her earning capabilities discounted to a present value where the individual’s contribution is based on a salary or wage. However, this type of analysis is often not performed because it is difficult to value a life. Cost-effectiveness analysis measures benefit or effectiveness in terms of units, such as life years saved or complication-free episodes. And lastly, Cost-utility analysis incorporates a utility or quality of life adjustment into the effectiveness metric.

Definition of Utilities (SLIDE 13)

What exactly is a utility? A utility is a quantified preference for a specific health state.

Expression of Utility (SLIDE 14)

How do we express utility? Utility measures yield a single value that reflect overall quality of life (QoL). They’re preference weighted measures that are used to produce point-in-time expression of well-being. They’re anchored or referenced on perfect health and death. For example, if we are examining different health states that might be associated with Human Papillomavirus, we might need to illicit preferences of patients to be normal, that is without disease, have asymptomatic Human Papillomavirus or HPV infection, have a health state that is intermediate between asymptomatic HPV infection and evasive cervical cancer, which is called Cervical Intraepithelial Neoplasia, or death.
Utility is used to impart quality of life component to an effectiveness value, such as life years gained; to establish quality-adjusted life years and we will discuss this idea further when we talk about cost-utility analyses using Human Papillomavirus cost-effectiveness determinations as a case study.

Influence of Compliance with Medication on Cost-Effectiveness  (SLIDE 15)

A key difference between efficacy and effectiveness that causes efficacy of a drug to change in the real world is patient compliance. In this table, Kozma and co-workers show that regardless of initial diastolic blood pressure in the left hand column, full compliance with the medication regimen would result in a cost per quality-adjusted life year or QALY that was about half that associated with partial compliance. So for example, if we look at the initial diastolic blood pressure of greater than or equal to 105 millimeters of mercury, full compliance would result in a cost per QALY of $4,850, while partial compliance would double the cost-effectiveness, meaning it would reduce the cost-effectiveness or make it worse, resulting in a cost per QALY of $10,500. Likewise, with a diastolic blood pressure that is lower than the initial blood pressure we discussed — 95 to 104 millimeters of mercury, full compliance would be about $10,000 or so, $9,880 per QALY, whereas partial compliance would result in a cost per QALY of $20,400.

Framework for Determining Costs  (SLIDE 16)

Costs are comprised of inputs — that is, type of cost, units of cost, and cost values and require adjustment for timing and uncertainty.

Cost/QALY Comparisons  (SLIDE 17)

To get an idea of various costs per QALY, you see here that it ranges from $69 per QALY for seat belts, to $140 per QALY for flu vaccine, to $26,000 per QALY for AZT for AIDS, to $50,000 per QALY for Human Papillomavirus vaccine, to $89,000 per QALY for a 55 mile per hour speed limit. A somewhat arbitrary threshold of $50,000 to $75,000 USD per QALY is the generally accepted figure for a cost-effective therapy.

Direct and Indirect Cost  (SLIDE 18)

The components of a pharmacoeconomic or cost-effectiveness analysis include costs and consequences. Costs can be divided into direct and indirect costs. Direct medical costs are those related to providing medical services, such as a hospital stay, physician fees for outpatient visits, drug costs and costs of adverse events, including the cost of the medication itself and any downstream adverse events that may arise as a result of drug administration. Direct nonmedical costs are those related to expenses such as transportation costs that are a direct result of the illness. Direct costs are most frequently included in a cost-effectiveness analysis, whereas indirect costs, those associated with changes of individual productivity are often not included in a cost-effectiveness analysis because they are difficult to obtain. Examples of indirect costs are lost time from work or absenteeism and unpaid assistance from a family member. Lastly, intangible costs, such as pain and suffering, may be included in the analysis.

Consequences  (SLIDE 19)

Consequences are the denominator of the equation — may be measured in terms of the monetary benefits, effectiveness, such as years of life saved, hospitalizations averted, complication-free episodes, and the like. They may also be measured with the incorporation of utilities yielding quality-adjusted life years or QALY.
**Average and Incremental Cost-Effectiveness  (SLIDE 20)**

There are two ways or performing or representing cost-effectiveness analyses, average cost-effectiveness and incremental cost-effectiveness. Average cost-effectiveness is the result of dividing mean total cost by outcomes and is typically represented as a per patient value. It is calculated as follows for each therapeutic option, cost divided by effectiveness. The average cost-effectiveness of each therapy is then compared and the one with the lowest cost per unit of effectiveness would be preferred. Although this type of analysis allows one to view the actual numbers involve in the calculation, average cost-effectiveness does not illustrate differences between alternative strategies. Thus, many researchers prefer to use or further explain the results of a CEA in terms of an incremental cost-effectiveness ratio – that is additional costs for additional benefit, which may be calculated as follows, delta “C” over delta “E” equals the differential in costs over the differential in effectiveness. The term incremental is commonly used to denote the additional costs and outcome of one intervention in comparison with another.

**Decision-Making in PE Analysis  (SLIDE 21)**

An incremental cost-effectiveness analysis is useful in the following two tradeoff instances: one, where the new strategy is more costly but expected to be more effective, or two, where the new strategy is less costly but less effective. The other quadrants in which a therapy is more costly and less effective or less costly and more effective would yield obvious choices and would not require that a CEA be performed.

**Perspective  (SLIDE 22)**

Another concept that is an important component of a CEA is that of perspective. The perspective of the analysis maybe that of society or a third party payer. The National Health Service or NHS and other nationalized payer systems suggest use of a societal perspective when CEAs are being performed. Here the benefits are often expressed in Quality Adjusted Life Years or QALY. However, shorter term outcomes, especially in countries like the US where the health care system is not nationalized and in fact is often covered at least partially by employers and patient turnovers are relatively rapid may be examined. Examples here might be MI avoided or complication-free episodes.

**Population Segmentation  (SLIDE 23)**

The population to be examined – patient age and race, such as the beta blocker approved only for African-American patients, all are important considerations and may be considered for sub-analyses in a cost-effectiveness analysis. Gender is another important component of population segmentation. For example, Weinstein and Stason showed that cost-effectiveness of antihypertensive agents improve as women aged but decline as men aged. This may reflect the propensity for women to develop cardiovascular disease later in life and the improved expected therapeutic effectiveness as a result. Also, the present state of screening for disease and assumptions about how screening processes may change over time in a particular health system may have an impact on the cost-effectiveness analysis.

**Discounting  (SLIDE 24)**

Future costs and effects are discounted to reflect the fact that in general, individuals and society have a positive rate of time and preference — that is in general, they prefer desirable consequences to occur earlier and undesirable consequences to occur later. Thus, future benefits are discounted to reflect the fact that they are worth less simply because they occur in the future rather than now. Similarly, future costs are discounted to reflect the fact that we prefer
them to accrue in the future rather than the present when the program extends over multiple years. The equation used to
determine discount rate is seen here, where PV is present value, FC is future costs and DF is the discount factor which
is dependent on the number of years into the future that expense is incurred characterized by N and the discount rate or
R.

Sensitivity Analysis  (SLIDE 25)

Sensitivity analyses are completed to test the feasible range of values for key variables in an analysis. This examines
the robustness of the analysis in that if small changes in the values of key variables cause a decision to change, the
results, and therefore the usefulness of the analysis may be suspect.

Uncertainty  (SLIDE 26)

There are two types of uncertainty in modeling, parameter uncertainty and structural uncertainty. Parameter uncertainty
uses sensitivity analysis and probabilistic uncertainty analysis. Structural uncertainty compares different structures with
the same or similar data and looks to see if one obtains similar results with these different structures.

Implications  (SLIDE 27)

“Given that the process of estimating subgroup-specific input parameters usually involves reducing sample size, it is
even more important to assess the implications of parameter uncertainty fully.” For the implications of this phrase, with
smaller groups of patients – that is, subgroups, we may be even less certain about input values, so we would need to do
even more sensitivity analyses around key parameters.

CEA Reporting Formats  (SLIDE 28)

These are just but two situations where one should expect to see a multitude of data relating to cost-effectiveness
analyses if one is evaluating a journal article for completeness and if one is using cost-effectiveness analyses to make
policy decisions.

CEA Reporting Formats (elements)  (SLIDE 29)

There are many different elements that one should expect to see when evaluating a journal article and/or making a
policy decision that has to do with cost-effectiveness analysis. One should have an adequate background; be able to
determine the viewpoint or perspective of the analysis, whether it be the patient, payer or society; the type of analysis,
cost-minimization, cost-benefit, cost-effectiveness, or cost-utility; the patient population, the comparators, the source
and quality of medical evidence such as randomized controlled trials, prospective or retrospective observational data, or
the published literature; the range in measurement of costs both in physical and monetary terms; and the measure of
benefit, such as life years gained or quality-adjusted life years.

CEA Reporting Formats (elements, cont’d)  (SLIDE 30)

Additionally, one should expect to see adjustments for timing of costs and benefits if this is a multiyear analysis.
Dealing with uncertainty, there should be multiple sensitivity analyses around key variables, incremental analysis of
costs and benefits and overall study results and limitations.
Issues in HPV CEA (SLIDE 31)

A Wallstreet journal article reported just a little under two years ago, quote, “A federal vaccine advisory panel unanimously recommended that 11- and 12-year-old girls receive a new vaccine designed to protect against cervical cancer.” These cost-effectiveness analysis for Human Papillomavirus vaccine to prevent against development of cervical cancer has proven to be very inflammatory in terms of cost, moral and ethical dilemmas and makes for a perfect case study for analyzing cost-effectiveness analysis use in formulary and policy decision making. And so I’ve chosen to use that as a case study.

Case Study: HPV Vaccine CEA (SLIDE 32)

Although there’ve been several cost-effectiveness analyses of this issue. The article that I will highlight at this time is by Sue Goldie, *Projected clinical benefits and cost-effectiveness of a human papillomavirus 16/18 vaccine*, published in Journal of National Cancer Institute in 2004. Goldie and colleagues developed a cost-utility model to evaluate cancer incidence and mortality, lifetime costs, life expectancy, and incremental cost-effectiveness ratios projected to be associated with cervical cancer and HPV vaccine in the prevention of cervical cancer. This case study will be used as an example of the use of cost-effectiveness analysis in medical decision making in the Cost-Effectiveness Analysis and Cost-Utility Analysis modules of this Distance Learning Program.

Summary (SLIDE 33)

In summary then, cost-effectiveness analysis or pharmacoeconomic analysis is the ratio of cost to effectiveness. It evaluates additional cost for additional unit of effectiveness and it may be used to make policy decisions among competing therapies with fixed resources available.

Thank you for your attention to this module.