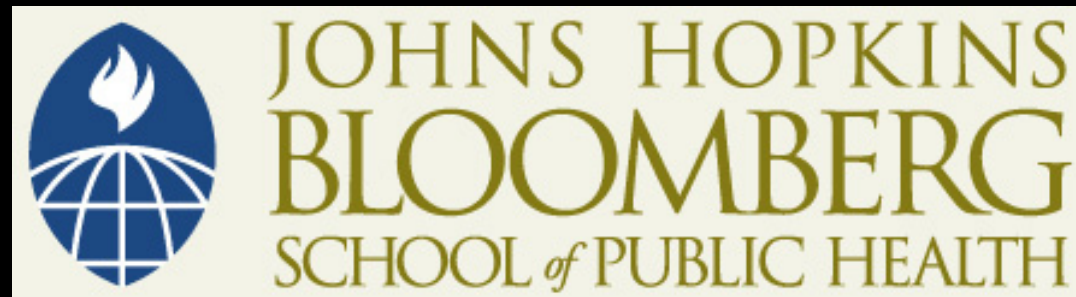


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REFERENCE CASE & GLOBAL RECOMMENDATIONS

Lecture 13

Kevin Frick

Background

- Have seen examples of techniques
 - Costing (discussed in CBA)
 - Discounting (discussed in CBA)
 - Health utility measurement
 - Sensitivity analyses
- Need to know whether there is any sense of preferred methodology

Important Readings

- Text
 - *Cost-Effectiveness in Health and Medicine*
 - Some basic material and some very detailed materials
- Supplementary articles from JAMA
 - 10/9/96: p 1172
 - 10/16/96: p 1253
 - 10/23-30/96: p 1339
- Summarized in Haddix et al. text
- Summary available on ISPOR website

What Is the Reference Case?

- An effort at standardization
 - Methods & assumptions
 - Facilitates comparisons of CE ratios
 - Reference case analysis should be done even when other analyses are of primary interest
- U.S. recommendations are just one example
 - Others on ISPOR website will be topic of discussion
- U.S. recommendations allow for judgment calls

What Do Standards Gain Us?

- Recognizable way to report results
- Recognized methods for judging the quality of a study
 - Understand that rules can be violated with justification
 - No scoring system to unambiguously rank criteria's importance in all cases
- Comparability of results across studies of disparate interventions
- Is there the potential to stifle innovation?
 - Have not observed this over time

Points in the Reference Case

- Perspective
- What are costs?
- What are effects?
- Patient time
- Fixed costs
- Market prices
- Inflation
- Transfer payments
- Time costs
- Future costs
- Measuring effectiveness
- Discounting
- Reflecting uncertainty
- Reporting
- Other issues

Point 1: Perspective

- **Single most important point**
- Societal
 - *Include all effects* including externalities
- Emphasize that CEA does not reflect important factors such as the ethical values of society's members
 - Should never apply ICERs mechanistically in a resource allocation process
 - Similar to the conclusion one would draw for CBA

Societal Measure of Effect

- QALYs are recommended
- QALYs imply equal weighting of effects across *similar* community members
 - Age is important consideration
- Health utility based on community preferences
 - Utilities based on community preferences are generally derived from responses to questions about how a condition will affect the respondent
 - Not individual patient preferences or preferences of all patients rather than the rest of society
 - Are community and patient preferences different?

Summary of Additional Recommendations

- Recommendations are intended to be...
 - Theoretically and logically consistent
 - Based on welfare economics (which drives CBA) where possible
 - Pragmatic and ethical
 - Ethical considerations led to the use of QALYs rather than WTP values
 - Pragmatic not to include all future costs and benefits
- Sometimes recommendations merely reflect the adoption of a common convention
 - Assume that “morbid time” is captured in health utility

Point 2a - General Framework for Numerator in CE Ratio

- Monetary measure of net resources used
- Cost of health care
- Patient time needed for intervention
- Caregiver time and associated costs
- Incidental expenses (child care/travel costs)
- Externalities affecting employers, coworkers, other family member, and others in society
- Externalities affecting the environment, criminal justice system, education system, etc.

Point 2b - General Framework for Denominator in CE Ratio

- Non-monetary measure of net change in quantity and quality of life due to health
- Includes morbidity effects on leisure and productive time
 - **These effects should not be monetized and included in the numerator**
 - **Work disability costs of illness**
 - Quality of life measure should be designed to capture *all disability costs*

Point 3 - Re-emphasis on Patient Time Issues

- Time seeking health care is counted in the numerator (\$)
- Morbidity time in the denominator (QALY)
- Recovery time could be either but *by convention* it is included in the denominator
 - What does this suggest about the importance of productivity?
 - What does this suggest about how people are responding to questions about the quality of life with various conditions?

Point 4 - Fixed Costs

- Should be left out unless different alternatives have different fixed costs
 - If fixed costs differ, are they really fixed?
 - Take a long run view
 - Remember to focus on incremental costs
- Important for total budget for a program or intervention even if they are not varying between alternatives

Point 5 - Use of Market Prices

- Generally market prices are acceptable
 - From a societal perspective, the goal is to use a measure that reflects opportunity costs
- May need to adjust market prices
 - Cost to charge ratios for hospital charges
 - Accounting values
 - Estimated micro-costing values
 - Similar to discussion regarding costs for CBA

Point 6 - Inflation

- Similar to inflation discussion in CBA
- Measure everything in constant dollars
 - Adjust to a base year using the (medical) CPI
- Recall what the CPI measures
 - Index equal to 1 in a base year
 - e.g. 1989 (0.98), 1990 (1), 1991 (1.03), 1992 (1.07)
 - Can either use CPI directly or use the inflation calculator at www.bls.gov

Point 7 - Transfer Payments

- Example: SSI payments
- Only include administrative costs in numerator
- Transfers represent the same amount of gain for one person and loss for another
 - Cancel out from societal perspective just as in cost-benefit analysis
 - Do not cancel from government's perspective
 - No consideration of the potentially different importance of a dollar to different individuals

Point 8 - Time Costs

- Use one market wage to value time?
- Reason for suggesting one wage
 - *By convention*, use the average wage conditional on age and gender *regardless* of employment status
 - Use sensitivity analyses to judge gender effect
 - Do not adjust for race, ethnicity or other characteristics
 - Ethical concerns

Point 9 - Future Costs (I)

- Costs that are the result of changes in longevity are very controversial
- Five types will be discussed
- (1) Intervention related - years lived anyway
 - Long run pharmaceutical treatment side effects
 - Include in the numerator
- (2) Unrelated costs during years lived anyway
 - If unrelated then don't include as nothing changed
 - Difficult to delineate these

Point 9 - Future Costs (2)

- (3) Intervention related during years added
 - Future complications from a heart transplant
 - Include in the numerator

Points 9 - Future Costs (3)

- (4) Unrelated medical during years added
 - For example, if prostate cancer is averted should include costs of later Alzheimer's
 - Conceptually, should include
 - Imposes a great burden on the analyst
 - Have to count all future costs
 - Do not need to count costs of specific conditions
 - For reference case, can include or exclude (big unresolved issue) and do sensitivity analyses

Points 9 - Future Costs (4)

- (5) Non-health care costs in added years
 - Conceptually similar to (4)
 - Should be included but even more impractical
 - Exclude these in the reference case

Point 10 - Measuring Health Effectiveness

- Measure in QALYs
 - Community-based preferences

Point 11 - Discounting

- Discount both the monetary and non-monetary effects
 - Otherwise will always pay to delay
 - Consider how this fits with the relevant group mattering
 - Any proposal to delay should measure the net costs of the delay
 - Discounting health suggests a tradeoff between future health and current consumption

Points 12 & 13 – More on Discounting

- For convention, discount both health and costs at the same rate
 - Again, if discount health effects using a lower rate the suggestion will always be to wait
- Rate to use
 - 3% discount rate
 - For sensitivity analyses use 0%, 5%, 7%

Arguments & Counters

- Prevention is different
 - No reason to say they should be valued more or less but, if feel a need to make an adjustment, change value
- Inflation
 - Adjust for inflation and discount
- Adjust discounting for uncertainty
 - Use expected discount rate
- The argument that it always pays to wait is irrelevant because sometimes money has to be spent within a given time period
 - Rarely have to spend money in limited time & would like to avoid issues anyway

Arguments & Counters (2)

- Proportional discounting ($b/(b+t)$)
 - Using standard discounting something one period later is always valued a $1/1.03$ regardless of when the “starting year” is
 - With proportional discounting the relative value changes with the starting year
- Real value of health benefits may not be constant
 - Change threshold but leave discounting alone
- Real cost of producing health changes over time
 - Adjust cost stream
- Individual discount rates
 - Use market rate because CEA’s purpose is prescriptive rather than descriptive

Some Empirical Work on Discounting (1)

- Hojgard et al. article on reading list
- Study of decision for watchful waiting versus surgery for patients with asymptomatic abdominal aortic aneurysms
- Surveyed vascular surgeons, GPs, internists, 60 year old men with and without abdominal aortic aneurysms
 - All were given same information

Some Empirical Work on Discounting (2)

- Gain years of life in the future
- Mortality risk with surgery
- Can calculate implicit discount rate
- Found that vascular surgeons had lowest discount rate (were most likely to recommend surgery) and internists were least likely
 - All discount rates are high (12% and above)

Point 14 - How to Reflect Uncertainty?

- Perform sensitivity analyses
 - Improved substantially since 1996
- Confidence interval calculations
 - High degree of improvement since the Panel's recommendations were made
- Simulations can be used for both issues

Point 15 - Reporting results

- How to summarize results
 - Report total costs and effectiveness
 - Report incremental costs and effectiveness
 - Use 3% and 5% discount rates
 - Report cases in order of increasing cost and effectiveness
 - Do not report any incremental results for dominated alternatives
 - Convention adopted to avoid confusion

Point 16 - Additional Suggestions

- Report results with no discounting
- Report life years gained
- Discuss robustness and sensitivity analyses
- Discuss generalizability of results and any ethical issues

When to Use CUA? (Drummond)

- QOL is *the important* outcome
- QOL is *an important* outcome
- Program affects *morbidity and mortality*
- Programs being compared have *different outcomes*
- Compare program to others *already evaluated with CUA*

When not to use CUA? (Drummond)

- Only *intermediate effectiveness* data can be obtained
- Effectiveness data shows that alternatives are *equally effective*
 - Need only cost minimization
- QOL important but can capture with single variable in easily understandable units
- Extra cost of obtaining utility data is prohibitive

Worldwide Guidelines

- General pharmacoeconomic guidelines
- Submission guidelines for formulary listing
- Journal publications
 - *BMJ only*

Pharmacoeconomic guidelines

Region	Countries
Oceania	New Zealand
Eastern Europe	Hungary, Poland, Russian Federation
Southern Europe	Italy, Portugal, Spain
Western Europe	Belgium, France, Germany, Netherlands, Switzerland
Northern Europe	Baltic, Finland, Ireland, Norway, Scotland, Sweden, England & Wales
Northern America	Canada, USA
Western Asia	

Formulary Listing Guidelines

Region	Countries
Oceania	Australia
Eastern Europe	
Southern Europe	
Western Europe	Belgium
Northern Europe	England & Wales
Northern America	Canada, USA
Western Asia	Israel

Pharmacoeconomic Guidelines - 1

- Title & year of document
- Affiliation of authors
- Main policy objective
- Standard reporting format included
- Disclosure of funding
- Target audience
- Perspective

Pharmacoeconomic Guidelines - 2

- Target population
- Subgroup analysis
- Choice of comparator
- Time horizon
- Assumptions required
- Preferred analytic technique
- Costs to be included

Pharmacoeconomic Guidelines - 3

- Source of costs
- Modeling
- Systematic review of evidence
- Preference for effectiveness over efficacy
- Preferred outcome measure
- Preferred method to derive utility
- Equity issues stated

Pharmacoeconomic Guidelines - 3

- Sensitivity analysis
 - Parameters and range
- Sensitivity analysis methods
- Presenting results
- Incremental analysis
- Total C/E
- Generalizability
- Financial impact analysis

Range of major policy objectives

- 1

- USA—Providing recommendations for conduct of C/E studies in order to improve their quality and encourage their comparability
- Baltic—Drug reimbursement and other state funding decisions
- Belgium—Provide guidelines to conductors and evaluators of PE studies

Range of major policy objectives

- 2

- Canada—Inform programmatic decision-making regarding the appropriateness and availability of health care interventions including drugs. Direct study design and provide standardized and reliable information to the target audience. Provide a template for final reports
- Finland—Reimbursement

Range of major policy objectives

- 3

- France—Provide credibility, quality and comparability
- Germany—Improve clarity of health economic studies
- Hungary—To support the decision-making process with sound C/E data and good quality economic study

Range of major policy objectives

- 4

- Ireland—Provide the Dept. of Health, the GMS payments board, and prescribers with CE information
- Italy—Pricing and reimbursement
- New Zealand—Provide HFA with methods to make resource allocation decisions
- Norway—Reimbursement

Range of major policy objectives

- 5

- Poland—Drug reimbursement
- Portugal—Improve the economic assessment methodology & information provided to decision makers
- Russian Federation—Regulatory basis for patient management protocols and formulary lists and schedules
- Switzerland—A list of criteria to be met for recognition of medical technologies/services as reimbursable

Range of major policy objectives

- 6

- Scotland—Assist submission to Scottish Medicines Consortium
- Spain—Formulate an initial proposal for methodological standards for economic evaluation used for pricing and reimbursement decision making
- Sweden—A list of criteria to be met for recognition of medical technologies/services as reimbursable

Range of major policy objectives

- 7

- Netherlands—Reimbursement
- England & Wales—To provide an overview of the principles and methods of assessment and appraisal within the context of the NICE appraisal process. The aims are to introduce the general methodological concepts underlying each stage of the appraisal process and to describe what is required of participants considering the submission of evidence to NICE.

Perspectives

- Societal (transparently broken down into relevant viewpoints)
- Health care system
- National Institute of Health & Invalidity Insurance/funder
- Patient and family
- Depends on the aims of the study/audience to whom study is addressed

Preferred Analytic Technique

- USA, Italy, Poland, Spain, Sweden, Netherlands, England & Wales—CEA or CUA
- Baltic, Belgium, Finland, France, Germany, Hungary, Ireland, Norway, Portugal, Russian Federation, Scotland, Switzerland—Variations on any of CMA, CEA, CUA, CBA, CCA. Need justification.
- Canada—CUA or CBA
- New Zealand-CUA only

Preferred Discount Rate

- Note—many variations
- 3%-USA, Italy, Sweden
- 3.5%-England & Wales
- 4%-Netherlands
- 5%-Baltic, Belgium, Canada, Finland, France, Germany, Hungary, Norway, Poland, Portugal, Russian Federation, Switzerland (many also list 2.5%)
- 6%-Scotland, Spain,
- 10%-New Zealand

Costs to Include

- Almost all focus on direct health care costs
- Report indirect separately
- Social services, spillover, family & patient
- All direct & indirect within health care. State production losses separately
- Only include productivity with justification
- Most comprehensive list possible or “all resources which are *non-trivial* in magnitude”
- Friction cost approach is mentioned

Rule of Thumb (opinion)

	Large Magnitude	Small Magnitude
Highly Variable	Include	????
Low Variance	????	Can be excluded

Submission Guidelines in US - 1

- Academy of Managed Care Pharmacy
- Devised by academic experts
- Main policy objective
 - Standardize formulary submission format, projecting budget impact
- Included a standard reporting format

Submission Guidelines in US - 2

- Main target audience
 - Pharmaceutical companies, insurers and reimbursers, health system administrators and managers
 - Different from Panel's goal to provide recommendations for conduct of C/E studies in order to improve their quality and encourage their comparability
- Perspective: Primary: Payer. Secondary: Societal
- Time Horizon: That is appropriate to the disease being studied and reflects the decision-making and financial and budget constrains of the organization.

Submission Guidelines in US - 3

- Does not specify preferred analytic technique
- Total medical & pharmacy costs and costs related to therapy
- Source of costs must be applicable to health plan
- Modeling OK, but must allow health plan to explore results

Submission Guidelines in US - 4

- Effectiveness is preferred
- Prefer final outcomes. Disease specific & generic HRQOL measures are acceptable.
- No preferred method to derive utility.
- 3% & 5% discounting with 0%-7% range
- For portability, suggest interactive model so health plan can put own data in.
- Financial impact for first three budget periods