Highlights from the Spring 2007
Applied Pharmacoeconomic and Outcomes Research Forum

The third Southern California Applied Pharmacoeconomic and Outcomes Research Forum was held May 14th at the University of California San Diego Faculty Club. The event was hosted by the Skaggs School of Pharmacy and Pharmaceutical Sciences and supported by a grant from Biogen Idec.

Forum attendees included managed care, government, medical center, academia, and pharmaceutical and biotech company representatives from Southern California. Attendees were invited because of mutual interest in expanding the practical application of pharmacoeconomic and outcomes research to enhance decision-making. Speaker slides are posted at http://pharmacy.ucsd.edu/news.shtm .

Topic
Our topic was **"Quality Adjusted Life Years (QALY's) for Decision Making: Views from Canada and the US"**

The Forum began with a brief tutorial illustrating the QALY concept by the session's moderator, Ted Ganiats, MD. For the purposes of our discussion, a QALY was defined as a way of measuring health outcomes that takes into consideration two priorities of health care: quality of life and life expectancy.

The Canadian Experience with QALY's

Decision makers in Canada have considered QALY's as a factor in their decision making process for pharmaceuticals for many years. Lesia M. Babiak, PharmD, MBA, Director, Federal Affairs & Health Policy, Janssen Ortho Inc. and formerly Associate Director, Drug Programs Branch for the government of Ontario presented an overview of the Canadian drug approval and reimbursement systems and the role of QALY's in decision making. Her remarks were based on subjective experiences and interviews with high-level decision makers who have been involved with using QALY's in Canada.

As background, Canada has a single Common Drug Review process which is dedicated to:

- Conducting objective, rigorous reviews of the clinical and economic evidence for new drugs in the assessment of cost effectiveness, and
- Providing formulary listing recommendations to the publicly funded drug plans in Canada (except Quebec)

Why are QALY's being used in Canada?

- Academic experts developed interest and have actively researched and published on QALY's since 1970's
- Clinicians involved in reimbursement decisions translated the academic concepts and made QALY's more accessible for reimbursement decision making
- Large single payers, were facing increasing cost pressures
- Pharmacoeconomic (PE) Guidelines issued provincially & nationally starting in the early 1990's incorporated QALY's

- QALYs are considered the gold standard for analyses because the concept combines benefits, side effects and QOL into one measure and allows for comparison across different drugs and diseases

What types of decisions are QALY's used for in Canada?

- *Formulary placement*
- Provincial drug plans
- Very limited use in Hospitals

Is using QALY's working?

- Effectiveness of QALY's in enhancing decision making has not been evaluated retrospectively
- Perceptions vary across the country about their effectiveness

Are there specific diseases where QALY's are more or less appropriate?

- Generally, QALY's are considered more relevant for chronic disease states, rather than acute or short term impairment
- QALY's are specifically useful in chronic pain, oncology and ADHD; They are not as useful for diseases with few symptoms (e.g. hypertension, elevated cholesterol)

Is there a threshold for an acceptable cost/QALY in Canada?

- There is no official threshold – a C$50,000/QALY is an arbitrary cut-off often deemed "acceptable;" it was previously based on the approximate annual cost of providing hemodialysis
- Threshold for acceptable cost/QALY currently does not differ between diseases
- There is a debate regarding the need for disease-specific thresholds (e.g. for drugs for rare diseases or oncology)

How aware is the public of the use of QALY's in decision making?

- Very limited awareness amongst Canadian public
- Some patient groups who are aware of their use question the C$50,000/QALY threshold
- 'Lay versions' of recommendations are in development that will refer to cost/QALY
- Limited to no awareness amongst prescribing community in Canada

What is the current situation regarding QALY usage in Canada?

Currently there is widespread uncertainty about QALY's for several reasons.

- Lack of confidence in the measures
    - Somewhat related to the debate regarding validity and accuracy of methods used to estimate of QALY's
- Concerns about the many assumptions made in modeling
- Too abstract for many decision makers
- Opaque; understandable to only a few individuals
- Despite concerns about accuracy & validity, QALY's rarely verified retrospectively
  Example: Eprex for treatment of anemia in patients on dialysis

  - 1990 evaluation by York Center for Health Economics, cost/QALY in the UK was £103,145
  - 2000 re-evaluation, cost/QALY now £17,067

- QALY's, when used at the time of product launch, could deny access to new advances. When examined in the context of real world experience, the product may become much more cost effective as in the above example.

- A recent panel of oncology reimbursement decision-makers failed to agree about value of economic evidence, although required, is not systematically considered (not sure what this bullet means?? – Lesia??)
  - Rocchi et al CADTH Policy Forum, 2007

- Established programs appear more comfortable with operating in a challenging multi-factorial decision making process that does not rely on cost/QALY index

- Early adopters of QALY's in Canada and some provinces appear to be moving away from the promise and simplicity of QALY's to employ a multi-factorial approach

Future of QALY's in Canada

Short term
- QALY's will be requested and preferred by some decision makers
- Actual use in decision making will continue to vary

Medium term
- A more active and public debate on the usefulness of QALY's is looming
- Publication of concerns with QALY's by the original thought leaders will undoubtedly result in pressure on national and provincial bodies to revisit the perceived value of QALY's

Expanding the Use of QALY's as a factor in decision making for pharmaceuticals in the U.S. – Pro's and Con's

QALY's are not required by any decision makers in the U.S. The Academy of Managed Care Pharmacy's Format for Formulary Submissions lists QALY's as one type of evidence that can be submitted to support the benefit and cost of a pharmaceutical.

Two speakers, Robert M. Kaplan PhD and Chris Leibman PharmD MS, briefly presented thoughts regarding the Pro's and Con's of using QALY's more broadly in the U.S, for decisions about pharmaceuticals.

Pro's

Dr. Robert M. Kaplan, Chair, Department of Health Services UCLA School of Public Health presented his thoughts regarding the advantages of using QALY's on a broader basis in the US.

The first question Dr. Kaplan suggested be considered was "how can we best use our resources to improve public health?" The US, as other countries, has a fixed level of resources with potentially infinite demand for health services. Thus, there is a need to make effective/efficient use of resources. This means setting priorities to make choices.

If widely different interventions are to be compared…..

- The measure of health must encompass not only differences in length of life, but differences in the quality of that life, such as symptom tolerability and daily functioning
- Thus… cost-utility analysis with effectiveness measured as QALY's is warranted

Currently, in the US, Medicare expenditures vary greatly among areas of the country. However, outcomes are not necessarily better in areas with higher expenditures. This has been reported previously in the literature and is consistent with Dr. Kaplan's recent experience with data in Los Angeles vs. San Diego Counties.

Dr. Kaplan gave several examples where cost/QALY has been successfully used at various levels of decision making, including as support for Medicare coverage decisions on the lower cost/QALY gained with lifestyle changes vs. metformin therapy in diabetics.

What has held us back from using QALY's on a broader basis for decision making? Distractions.

Although there is agreement on some core issues surrounding QALY's, areas of particular disagreement exist and distract us from using QALY's.

- Distractions based on:
  - disagreements regarding which measures are best?
  - differences in general philosophy of outcome measurement
    - » Generic vs. disease specific
    - » Psychometric vs. utility based
  - Disciplinary differences – statistics, economics, medicine, psychology, anthropology….
  - Concern about response shift – preferences of patients and non-patients differ therefore preference weights used to construct QALY's may, be difficult to interpret

    Dr. Kaplan questioned the evidence supporting this last point (response shift) and showed two studies that suggest preferences from patients and non-patients are similar. Moreover, preferences from subjects in different countries also appear similar.

Difference in rating methods for constructing QALY's (e.g. Standard Gamble, Time Trade-Off) were also cited as reasons to question the usefulness of QALY's. Dr. Kaplan suggested that perhaps we should think of these as another QOL researcher (John

Ware PhD) has suggested "…different approaches as brand names of products designed to measure the same underlying construct… health."

As evidence of the similarity of methods to assess QALY's Dr. Kaplan cited a recent study where several measures of QALY's were utilized. All captured the clinical change that occurred in the trial, only the absolute value of the change differed.

Dr. Kaplan's Concluding Thoughts

1. Utility based measures are available to estimate the impact of pharmaceutical products on QALY's
2. Generic methods allow the comparison of investments in drugs relative to alternative healthcare investments
3. There are very few applications at present
4. Further development of these methods is needed for studies on pharmaceutical regulation

Con's

Dr. Chris Leibman, Senior Director, Pharmacoeconomics, Elan Pharmaceuticals Inc. presented on the disadvantages of using QALY's on a broader basis in the USA.

Dr. Leibman questioned the usefulness of QALY's for pharmaceutical decision making using three questions:

1. *Are QALY's credible?*
2. *Are QALY's understandable?*
3. *Do QALY's provide actionable information?*

1. *Are QALY's Credible?*

- Not all QALY's are created equal since different groups are valuing them
- Example: Alzheimer's Disease (AD)
  - Proxies often measure and value AD patient's health status
  - Is this an accurate reflection of the AD patient's preferences?
  - Methods are needed to properly account and aggregate the health benefits derived by the AD patient, their caregivers and their families
- Instead of valuing all QALY's equally, we may want to weight QALY's for different groups and interventions differently

2. Are Decisions Made with QALY's Understandable?

- Many interventions are funded despite higher than "traditionally acceptable" cost per QALY ratios, for instance:
  - The *minimum* estimates for enzyme replacement therapy for Gaucher's Disease range between $49,000/QALY and $147,000/QALY
  - The median Cost/QALY of commonly performed blood safety interventions is $355,000/QALY
- Medicare also covers technologies with high cost/QALY estimates:
  - Lung-volume reduction surgery: $98,000-$330,000/QALY
  - PET for Alzheimer's disease: Over $500,000/QALY
- Even within the same therapeutic area, different studies can produce sufficiently different results to cast doubt

- Cost/QALY estimates for hormone replacement therapy range from over $100,000/QALY to less than $10,000/QALY

Despite cost/QALY estimates that were greater than the commonly accepted threshold, the National Institute of Clinical Effectiveness (NICE) in the UK recommended three Acetylcholine Esterase Inhibitors for use in a subset of AD patients. The decision was based on other factors including specialist clinic assessment of cognitive, global, and behavioral functioning (ADL's and QOL), caregiver input and physician judgment of likelihood of compliance.

3. *Do QALY's Provide Actionable Information?*

Most payer questions regarding pharmaceuticals focus on 'comparative effectiveness' of products. Payers want to be able to make informed decisions about the effectiveness and costs between a number of treatment alternatives that are available for a particular disease or condition.

For example the Drug Effectiveness Review Project (DERP) is a collaboration of organizations that have joined together to compile the best available evidence in order to better inform public policy and decision makers in local settings. Their focus is on effectiveness and safety comparisons between drugs in the same therapeutic class.

Historically cost/QALY analyses have been used to value programs with widely different outcomes. Using cost/QALY's to answer the comparative effectiveness questions of payers is a misapplication of QALY's, since it requires evaluation of interventions with similar outcomes.

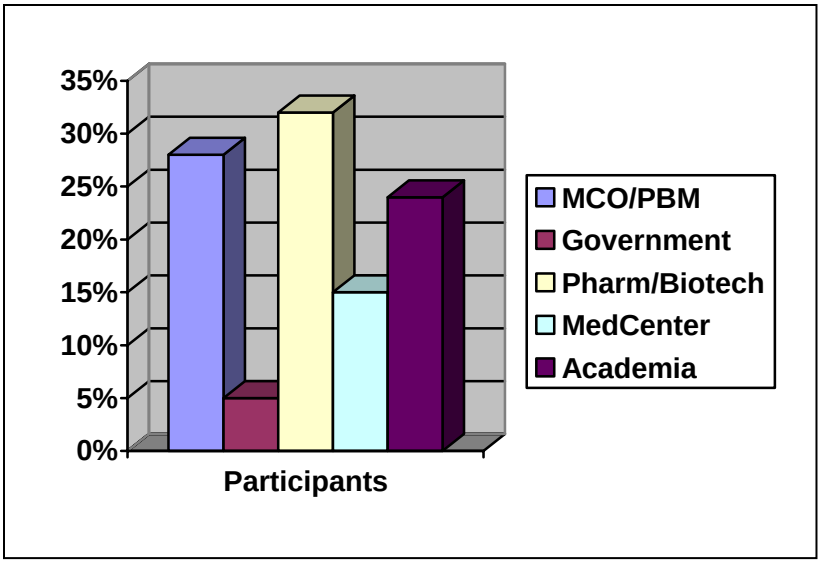
Dr. Leibman's Concluding Thoughts

- QALY's are useful as a descriptive rather than a prescriptive tool
  - QALY's are one important piece of information among others that should be considered
  - "Cost-consequence" approach to decision making may be preferred
- QALY thresholds need to be created according to perspective (and perhaps by disease state)
- The common, natural denominator for cost-effectiveness analyses within treatment classes should be used, rather than constructing QALY's

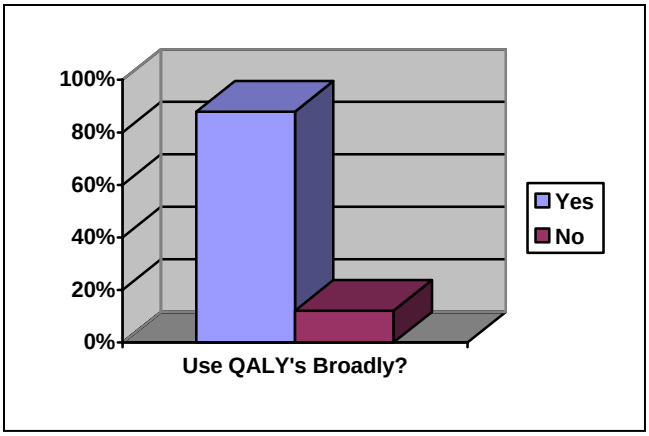
Participant Opinions

Participants gave their opinions about expanding the use of QALY's in the U.S..

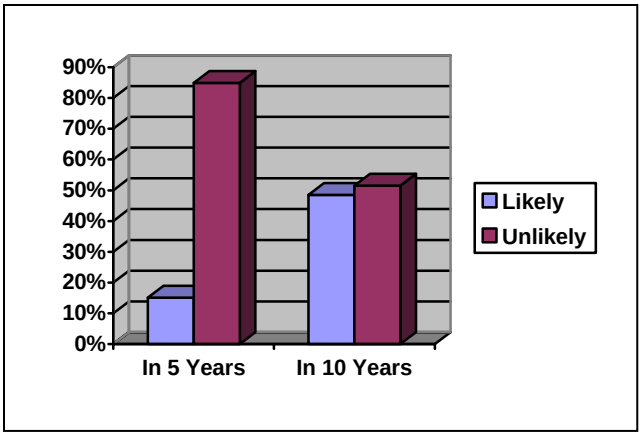
The majority (87.9%) agreed that QALY's should be used broadly as a factor in decision making for pharmaceuticals in the US. However, only 15% believed broader usage was likely to occurring the next five years while almost half (48%) thought broader usage was likely within a ten year horizon. Not reflected in these results is the Forum discussion that overwhelmingly indicated that QALY's are only a single piece of information to help inform multi-factorial decisions about pharmaceuticals.



Should QALY's be used broadly as a factor in decision making for pharmaceuticals in the US?

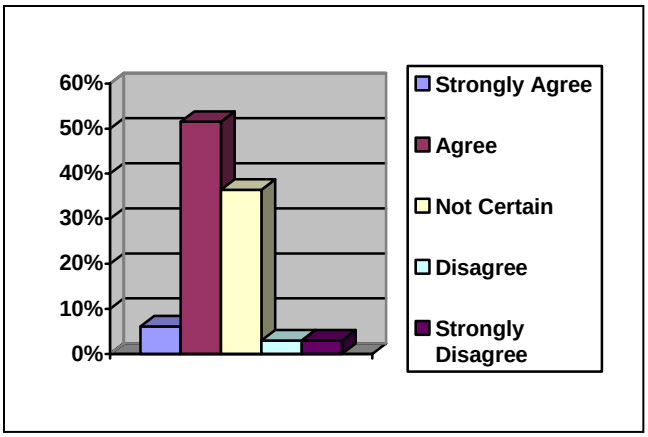


Likelihood of U.S. having broader use of QALY's for decision making among pharmaceuticals?



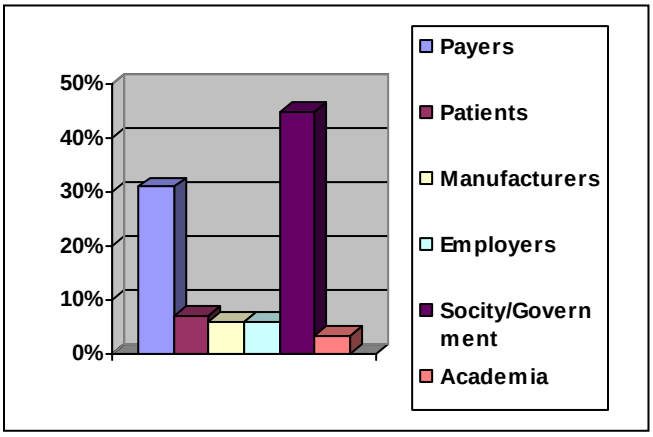
The majority (57.6%) of participants agreed that a centralized body or group should be responsible for evaluating the QALY's produced by new pharmaceuticals. However, over one-third were uncertain about this.

A centralized body or group in the U.S. should be responsible for evaluating the QALY's produced by new pharmaceuticals?

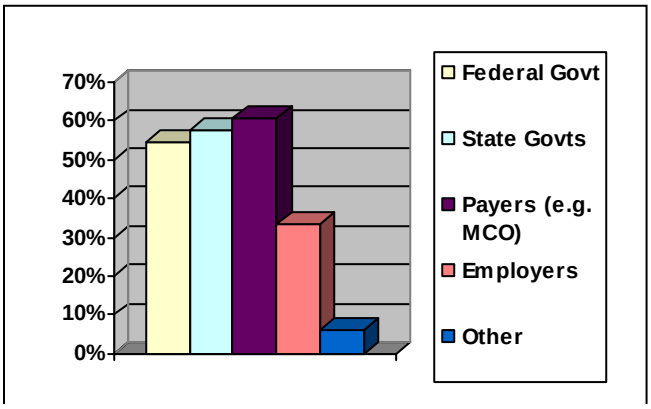


If QALY's were to be used on a broader basis in the US most participants believed society/government (44.8%) and payers (31.0%) would receive the greatest benefit. Approximately 60% of participants indicated that the direct payer groups (federal and state government and payers (e.g. insurers)) should be responsible for including QALY's in decision making for pharmaceuticals.

Using QALY's on a broader basis in the U.S. would be of <u>greatest benefit</u> to:



Who should be responsible for including QALY's in their decision making for pharmaceuticals?



<u>Other:</u>
- No one - However QOL should be used and considered alongside clinical and economic outcomes;
- Pharma, Biotech and Clinicians (MDs and PharmDs)

Purpose of the Forum

The number of individuals in the Southern California region with interest in pharmacoeconomics (PE) is growing rapidly across the healthcare continuum - from those involved with creation of PE data within pharmaceutical and biotech companies to those incorporating results into decision making within a plethora of managed care organizations. The local expertise provides an excellent opportunity to gather individuals to debate and propose solutions that are vetted from multiple perspectives – not just individual silos defined by employer.

The Applied Pharmacoeconomic and Outcomes Research Forum was created to facilitate this cross-perspective communication. The goals of the forum are to:

1. Discuss commonly encountered obstacles to conducting or utilizing results of applied pharmacoeconomic studies and to explore solutions from various perspectives of the health care system
2. Create an environment and foundation for fostering the evolution of a California-wide Pharmacoeconomic and Outcomes Research Interest Group

Our committee members representing major perspectives of the healthcare system are:

Charles Daniels, R.Ph., Ph.D.
UCSD Healthcare Department of Pharmacy

Ted Ganiats, MD
UCSD School of Medicine

Jan D. Hirsch, R.Ph., Ph.D.
UCSD, Skaggs School of Pharmacy & Pharmaceutical Sciences

Mirta Millares, Pharm.D., FCSHP, FASHP
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Anthony P. Morreale, Pharm.D., MBA, BCPS
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Aequitas

Robert Schoenhaus, Pharm.D.
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Ray Townsend, Pharm.D.
Elan Pharmaceuticals, Inc.

The Forum is a single effort amongst our larger intentions to promote the application of pharmacoeconomic and outcomes analyses for enhanced decision-making on the relative value of pharmaceuticals, medical services and technology for all healthcare systems. Other activities include education, training, research, and dissemination activities, including Continuing Education Programs to support this goal.

The Steering Committee would once again like to thank Biogen Idec for their support of the May 2007 Forum.