

FORUM



## HEALTH STATE UTILITY VALUES: MEASURING, MODELLING, AND MAPPING

Tuesday, 11 November 2014



ISPOR Task Force

FORUM



**Moderator**



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## HEALTH STATE UTILITY VALUES: MEASURING, MODELLING, AND MAPPING

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## HEALTH STATE UTILITY VALUES: MEASURING, MODELLING, AND MAPPING

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### WHY IS ISPOR DOING THIS NOW?

The quality of health state utility value estimates is critical to the quality of cost-utility analyses, and to the health technology assessment decision-making processes which determine whether new health interventions are made available to patients in many countries

ISPOR Vision 2020 Research Committee identified “Estimating HRQL weights (health state utilities) for cost-effectiveness analysis” as one of the top two priorities

***Guidance is lacking and good research practices task forces should be convened***

<http://www.ispor.org/ISPOR-Good-Practices-for-Development.pdf>



## HEALTH STATE UTILITY VALUES: MEASURING, MODELLING, AND MAPPING

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#### OUR WORK WILL BE VALUABLE FOR:

- ❖ Researchers involved in the design, implementation and analysis of studies to estimate HSUVs
- ❖ Guidance on best practices – to provide high quality HSUV estimates
- ❖ Those responsible for receiving, reviewing and decision making based on these analyses



## HEALTH STATE UTILITY VALUES: MEASURING, MODELLING, AND MAPPING

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#### TASK FORCES

- ❖ Mapping to Estimate Health State Utility Values from Non-preference Based Outcomes Measures for Cost per QALY Economic Analysis
- ❖ Measurement of Health State Utility Values for Economic Models in Clinical Studies

## FORUM



### Chair



**Allan J Wailoo, PhD,**  
Professor of Health Economics, SchHARR, University of Sheffield and Director, NICE Decision Support Unit, Sheffield, UK



### Use of Mapping to Estimate Utility Values from Non-Preference Based Outcomes Measures for Cost per QALY Economic Analysis - Good Research Practices Task Force



### Use of Mapping to Estimate Utility Values from non-Preference Based Outcomes Measures for Cost per QALY Economic Analysis - Good Research Practices Task Force

## FORUM

#### Leadership Group

**Marc Botteman, MSc, MA,** Partner, Pharmerit International, Bethesda, MD, USA

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## Use of Mapping to Estimate Utility Values from non-Preference Based Outcomes Measures for Cost per QALY Economic Analysis - Good Research Practices Task Force

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#### Why a Good Practice Guide now?

- ❖ Mapping is used increasingly in economic evaluation
- ❖ Complex area due to inherent characteristics of utility instruments
- ❖ Methods used are hugely variable
- ❖ Growing evidence of the performance (and underperformance) of different approaches
- ❖ Great uncertainty and confusion about how to interpret and use results
- ❖ Requirement for improved reporting standards to aid transparency and confidence in methods
- ❖ Uncertainty in estimates and variability at the patient level need to be appropriately considered



## Use of Mapping to Estimate Utility Values from non-Preference Based Outcomes Measures for Cost per QALY Economic Analysis - Good Research Practices Task Force

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- ❖ **What the guideline WILL cover**
  - ❖ What “mapping” is and when it should be considered
  - ❖ Good practice in estimating health state utilities from IPD
  - ❖ Key features of the estimation dataset.
  - ❖ The type of statistical models
  - ❖ Reporting standards
  - ❖ Validation
  - ❖ The use of estimates in cost effectiveness analysis



## Use of Mapping to Estimate Utility Values from non-Preference Based Outcomes Measures for Cost per QALY Economic Analysis - Good Research Practices Task Force

### FORUM

- ❖ **What the guideline will NOT cover:**
  - ❖ How to assess whether a specific utility instrument is appropriate or not in the assessment of a particular technology or in a particular disease area.
  - ❖ Expert opinion as a means of linking one instrument to another.
  - ❖ Measurement of HRQL in general within clinical studies



## Use of Mapping to Estimate Utility Values from non-Preference Based Outcomes Measures for Cost per QALY Economic Analysis - Good Research Practices Task Force

### FORUM

#### Timeline

Activity:	Date:
Proposal reviewed by the ISPOR Health Science Policy Council	May 2014
ISPOR Board of Directors approves proposal	June 2014
Finalized outline and proposed roles	Sept 15, 2014
Draft development	October - February
Forum Amsterdam	Nov 11, 2014
Draft sent to primary reviewers	March 2015
Forum Philadelphia	May 18, 2015
Revise draft based on comments and forum	June 2015
Draft sent to review group	July 2015
Revise draft	August - September 2015
Draft sent to ISPOR membership for review	October 2015
Revise draft	November 2015
Draft submitted to <i>Value in Health</i>	December 2015



## Use of Mapping to Estimate Utility Values from non-Preference Based Outcomes Measures for Cost per QALY Economic Analysis - Good Research Practices Task Force

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### Outline

1. Background
2. Introduction
3. Pre-modelling considerations
4. Modelling and data analysis
5. Reporting of results
6. The use and interpretation of results from mapping models.
7. Conclusions



### Pre-modelling considerations

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Consideration needs to be given to the proposed use of any mapping study and the range of data available. Key considerations include:

- ❖ What is the decision problem that the cost effectiveness analysis aims to address and to what extent does existing utility evidence address this issue? Mapping is most often seen as a means of spanning an evidence gap so a clear statement of the nature of this gap is required.
- ❖ If the mapping study is being undertaken as a stand-alone piece of analysis i.e. not explicitly linked to a specific cost effectiveness analysis, consider the issues that the analyst must be aware of in order that the mapping will be useful and relevant to future CEAs.



## Pre-modelling considerations

### FORUM

Consideration needs to be given to the proposed use of any mapping study and the range of data available. Key considerations include:

- ❖ Specifying the question that the mapping study will address. This will help to inform decisions about whether simple descriptive statistics will be sufficient (e.g. the mean utility score for subgroups defined by broad classes) or if formal statistical modelling of some type is required.
- ❖ Selection of an estimation dataset; characteristics that should be investigated and reported on, whether it should be used in its entirety or “split” to create a validation set, and limitations.



## Modelling and data analysis

### FORUM

- ❖ In many situations it'd be appropriate and necessary to estimate a statistical model of the relationship between a series of explanatory variables and the target health utility value. This is the area of mapping that is least well performed because simple methods have been shown to be systematically biased. We will:
- ❖ Describe the types of statistical models that analysts may wish to select from, their key features (in non-technical terms) and refer to relevant literature for full details. We shall cover:
  - ❖ “Direct” and “Indirect” estimation methods.
  - ❖ The issues that should guide model selection





## Modelling and data analysis

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- ❖ Dealing with repeat observations
  - ❖ It is typical of many clinical studies that can be used in mapping studies that patients provide multiple observations.
  
- ❖ Other issues with model estimation that we will consider
  - ❖ Convergence of simulation estimation methods, Bayesian analyses, How to undertake stage 2 of indirect methods.



## Reporting of results

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**Reporting of results**, must include

- ❖ Features of the estimation dataset
  
- ❖ Justification of model type(s) selected
  
- ❖ Justification for covariates used and how specified
  
- ❖ Model performance including appropriate methods for reflecting model fit across the entire range of disease and where the model is extrapolated beyond the data/where data is sparse.



## Reporting of results

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### Reporting of results, must include

- ❖ Comparing and selecting from different model types and specifications.
- ❖ The role of formal validation with a clear statement on what “validation” really tests and its limitations.
- ❖ Comparisons with other studies that can be made (and those that cannot).
- ❖ Recommendations for reporting of information on parameter estimates, uncertainty, measures of variability, model performance for optimal model and other models tested but rejected.



## The use and interpretation of results from mapping models

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- ❖ This section is specific to analysts using mapping studies in CEA
  - ❖ How to obtain estimates of mean utility for the health states required in a decision model / trial based economic evaluation.
  - ❖ How to reflect variability on those CEA analyses that require it (patient level simulation models and potentially trial based analyses).
  - ❖ Methods for the reflection of parameter uncertainty in mapping estimates
  - ❖ Methods to reflect structural uncertainty

## FORUM

### Co-Chairs



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## Measurement of Health State Utility Values for Economic Models in Clinical Studies - Good Practices Task Force



## Measurement of Health State Utility Values for Economic Models in Clinical Studies - Good Practices Task Force

## FORUM

### Leadership Group

**Vasily Belozeroff, Health Economics Director, Global Health Economics, Amgen Inc., Thousand Oaks, CA, USA**

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**Jennifer Petrillo, PhD,** Associate Director, HEOR, Global Market Access, Biogen Idec, Cambridge, MA, USA



## Measurement of Health State Utility Values for Economic Models in Clinical Studies - Good Practices Task Force

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### Objectives

- ❖ Identify & discuss issues inherent in the collection of HSUVs for economic models in clinical studies
- ❖ Provide researchers with an understanding of how to analyze & resolve the issues



## Measurement of Health State Utility Values for Economic Models in Clinical Studies - Good Practices Task Force

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### Objectives

- ❖ Make recommendations for
  - ❖ Early planning of utility data collection within a product development program
  - ❖ Design of utility data collection during protocol development for a planned clinical trial
  - ❖ Design of supplementary / alternative studies, including prospective / cross-sectional observational studies
  - ❖ Analyses and reporting to make best use of the data for economic models
- ❖ Applicable for
  - ❖ Pharmaceuticals, medical devices, diagnostics & vaccines
  - ❖ Public- and private-sector funded trials



## Measurement of Health State Utility Values for Economic Models in Clinical Studies - Good Practices Task Force

FORUM

### Outline

1. Background
2. Introduction
3. Appropriateness of clinical trials for measuring utilities for economic models
4. Early planning of utility data collection within a product's research and development program
5. Design of utility data collection during protocol development for a planned clinical trial
6. Design of prospective or cross-sectional observational studies for utility estimation
7. Other study types for estimation of HSUVs
8. Data analysis and reporting
9. Conclusions



## Measurement of Health State Utility Values for Economic Models in Clinical Studies - Good Practices Task Force

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What the guideline will NOT consider

- ❖ Utility estimates for economic analyses alongside trials
  - ❖ E.g. using longitudinal utility data to calculate QALYs directly (outside of an economic model)
- ❖ Measurement of HRQL in general within clinical studies
  - ❖ But may include a statement as to whether utility measures (e.g. EQ-5D) can/should be used to demonstrate differences in HRQL from baseline or by treatment group (as a substitute for disease-specific or generic HRQL measures e.g. SF-36).
- ❖ Mapping



## Measurement of Health State Utility Values for Economic Models in Clinical Studies - Good Practices Task Force

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### Timeline

Activity:	Date:
Proposal reviewed by ISPOR Health Science Policy Council	May 2014
ISPOR Board of Directors approved proposal	June 2014
Assign sections of the manuscript to the task force members	July 2014
Draft manuscript sections	September - October 2014
Joint Forum Amsterdam	November 11, 2014
Draft manuscript reviewed by task force members	November- December 2014
Manuscript draft sent to ISPOR Primary Review Group	January 2015
Revised manuscript sent to Review Group	March 2015
Presentation at ISPOR Annual International Meeting, Philadelphia	May 2015
Manuscript revised based on comments received at presentation	June 2015
Review by ISPOR membership	August 2015
Revisions to manuscript based on review	September 2015
Manuscript submitted to Value in Health	November 2015



## Appropriateness of clinical trials for measuring HSUVs for economic models

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- ❖ Which of the HSUVs required for the model are feasible to collect in the trial?
  - ❖ In view of the number of participants, planned follow-up period and feasibility of collecting utility data for health states and events of interest
  - ❖ Are estimates for acute events are required; Is it feasible to collect these data?
- ❖ Will trial participants be able to complete utility assessments?
  - ❖ Could proxy respondents could be used?



## Appropriateness of clinical trials for measuring HSUVs for economic models

### FORUM

- ❖ Factors influencing the generalizability of the trial population to routine clinical practice
  - ❖ And how these may be addressed
- ❖ Notes:
  - ❖ Single arm trials may also provide an opportunity for utility measurement (although not direct within-trial estimation of differences between treatments)
  - ❖ Consider heterogeneity in type of previous event, combinations of events, time since event
- ❖ Are supplementary / alternative studies appropriate?



## Early planning of utility data collection within a product's research and development program

### FORUM

- ❖ Selection of a suitable utility instrument
  - ❖ Collation of qualitative and quantitative empirical evidence for alternative instruments - top-level steps to establish validity and responsiveness of alternative instruments (disease-specific and generic)
- ❖ Identification of the HSUVs required for the economic model
  - ❖ Early economic model conceptualization
  - ❖ Importance of new HSUV research to model results



## Early planning of utility data collection within a product's research and development program

### FORUM

- ❖ Consideration of whether and which study(ies) within the planned clinical development program should include utility measures
  - ❖ Which trials will be able to provide the required HSUVs
  - ❖ Could phase II trial(s) be used e.g. to investigate validity and responsiveness of a measure or observe health states occurring beyond the end of the Phase III trial follow-up period
- ❖ Identification of data gaps & planning of additional research



## Design of utility data collection during protocol development for a planned clinical trial

### FORUM

- ❖ Selection of utility instrument & respondents
- ❖ Timing and frequency of assessments
  - ❖ Chronic health states (with stable or declining utility)
  - ❖ Acute events (utility and duration)
  - ❖ Adverse events
- ❖ Mode of administration
  - ❖ Flexibility vs standardization across patient sample and time





## Design of utility data collection during protocol development for a planned clinical trial

### FORUM

- ❖ Period of follow-up
  - ❖ & which patients are followed up
- ❖ How to address a heterogeneous population
  - ❖ E,g, type of previous event, combinations of events, time since the event
- ❖ Identification and resolution of any issues specific to the trial, study or model requirements



## Design of prospective or cross-sectional observational studies for utility estimation

### FORUM

- ❖ Selection of study type
  - ❖ Prospective, cross-sectional, etc.
- ❖ Selection of study population
  - ❖ Patients and/or proxy respondents
  - ❖ Sample size
- ❖ Period of follow-up
  - ❖ & which patients are followed up
- ❖ Selection of utility instrument and timing of assessments, mode of administration etc. (referred to previous sections)



## Other study types for estimation of HSUVs

### FORUM

- ❖ Guidance on
  - ❖ Other methods which have been used
  - ❖ Whether & under what circumstances they are / are not appropriate
- ❖ Direct elicitation
  - ❖ Valuation of vignettes by general population samples
  - ❖ Standard gamble / time trade-off
- ❖ Elicitation from healthcare professionals
  - ❖ As this has been used in the past
  - ❖ Not recommended



## Data analysis and reporting – Possible topics

### FORUM

- ❖ Application of value sets in the context of multinational trials
- ❖ Variability in response across the world in multinational trials
- ❖ Metrics (absolute utility vs change from e.g. baseline)
- ❖ Missing data and non-random censoring
- ❖ Floor and ceiling effects
- ❖ Correction of bias (generalizability to the population in routine clinical practice)



## Data analysis and reporting – Possible topics

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- ❖ Simple summary statistics vs regression
- ❖ Association with categorical vs continuous clinical outcomes
- ❖ Capturing correlations e.g. between better and worse health states in PSA
- ❖ Reporting to maximize value for future models
- ❖ Comparing/combining utility estimates measured in clinical studies with values from other studies (e.g. published literature)



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