

A Review of Quality of Life Instruments for Decision Making

There are many factors to consider when deciding on which multi-attribute utility instrument (MAUI) to use for the assessment of quality of life: responsiveness to the anticipated treatment and disease effects on quality of life; respondent questionnaire burden; analyst burden; acquisition costs; whether to use a 'generic' or 'condition specific' MAUI; and whether it will assist in affecting health care decision making. A recent Health Technology Assessment by Longworth et al (2014) explores some of these factors for three of the most widely used MAUIs – the EQ-5D-3L, the HUI and the SF-6D (derived from the SF-36). The project conducted by researchers at Brunel University London and the University of Sheffield in the UK reviewed studies in four key clinical areas: vision impairment, skin conditions, hearing impairment and cancer.

One of the key aspects of the project was a systematic review to assess the evidence on the psychometric properties (in terms of responsiveness, known groups analyses, convergent validity and reliability) in all four clinical areas. For the cancer aspect of the review, a total of 98 studies were included among which breast (n=11) and colon (n=10) provided the most papers. Of the MAUIs used, the majority of studies reported on the use of the EQ-5D (n=71), followed by the HUI-2/3 (n=24), and the SF-6D (n=3). Given the small number of studies covering the SF-6D, no conclusions are made regarding its properties relative to the other MAUIs.

How did the EQ-5D and HUI perform? Generally, both performed well on the measures used. Studies which allowed

for testing of known group analyses and convergent validity for the EQ-5D showed satisfactory results; in many cases the EQ-5D was able to discriminate between groups. Responsiveness measures indicate the EQ-5D can detect appropriate changes over time, but these were not always statistically significant. There was some evidence of reliability for the EQ-5D, even though this was not often available, and mainly inferred from patient groups where scores were expected to be stable, or not differ. Across cancer types there was variability in the performance of the EQ-5D on these various psychometric properties, eg. there was evidence to support good responsiveness and convergent validity in breast cancer, but in colon cancer responsiveness of the EQ-5D was not supported in the only study in which it was tested. An extensive discussion of the properties for each of the cancers for which evidence is available can be found in the online reference. For the HUI-3, there was evidence to support its ability to discriminate between groups, and for it to be responsive to clinical and treatment effects. Studies of inter-rater reliability also found this to be satisfactory; which is of potential relevance in paediatric, palliative or advanced care settings where carer completion might be appropriate.

This review provides valuable evidence to better inform the choice of MAUI for use in assessing quality of life in cancer clinical trials. The availability of cancer specific evidence on instrument responsiveness, validity and reliability provides an important input to the trial design process.

To access the full report go to:

http://www.journalslibrary.nihr.ac.uk/data/assets/pdf_file/0008/108368/FullReport-hta18090.pdf

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TROG celebrates International Clinical Trials Day

On Wednesday May 20, in honour of International Clinical Trials Day, TROG trial participant, Carol (pictured), shared her story to raise awareness about the importance of clinical trials.



Photo of Carol courtesy of Joerg Lehmann

After being diagnosed with Ductal Carcinoma In Situ (DCIS) in 2010, Carol decided to take part in the TROG 07.01 (DCIS) trial, while undergoing radiotherapy treatment. In this study, which has now completed recruitment, researchers are looking for

better ways to treat people with DCIS by testing whether an additional dose of radiation called a ‘boost’, improves the chances of the cancer not returning to the breast.

“I decided to join a clinical trial, simply because I thought, well, I’m on this journey and if I can help research and development, then I would do that,” Carol said.

“It was an easy way of being part of something bigger and an easy way of helping future generations have better access and better treatment.”

“One of the things that made me want to take part in the trial was, two of my friends were both diagnosed with cancer, just before I was and neither of them are here anymore. So even though it was a different cancer to the one I had, I felt I should do something because I owed it to them.”

“The benefits of being seen every six months and knowing that someone is monitoring you closely, is a great reassurance. And, as it transpired, I had another form of cancer in my

back which was discovered during one of my visits – so being on a trial has been a massive advantage.”

“I hope that by sharing my story, I can help other people realise that clinical trials are a really good thing to be part of. I believe that things come to challenge us in life and it’s not what you get, it’s how you deal with it that matters.”

TROG celebrated 2015 International Clinical Trials Day by holding an information stall at Calvary Mater Newcastle. The event is held every year around the world to mark the world's first clinical trial which took place in 1747.



Consumers as Research Partners: Presentation to Sydney Catalyst

On Wednesday 29th April, Richard De Abreu Lourenco, research fellow at CHERE, and Kim Parish, consumer representative from the Breast Cancer Network Australia, gave a joint presentation at the Sydney Catalyst 2015 Post Graduate and Early Career Research Symposium on their experience of successfully involving consumers in research. The presentation stemmed from a

research project conducted as part of Richard’s PhD which examined women’s preferences for managing the risk of breast cancer recurrence. Using an interview style presentation, Kim and Richard took the audience through what they found to be the key points on involving consumers in research projects, including:

1. Work with an umbrella consum-

er group in a relevant area.

2. Engage with the consumer group, and the consumer representative/s, early in the research.
3. Consumer representatives have a wealth of experience to offer the research project; respect their health history but recognise they have more to offer beyond that history;
4. Treat consumer representatives

Consumers as Research Partners (cont.)

- as you would any other member of the research team;
- 5. Have a kick-off-meeting so everyone can meet;
- 6. Provide face-to-face training on the proposed research methods and approaches;
- 7. Communicate regularly and be upfront in your mutual expectations; and
- 8. Be open to input and provide

feedback on how contributions from the consumer will be/are being used.

The emphasis of the presentation was the need to shift from the perception that the main reason for including consumers in research is to meet the requirements of funding organisations to recognising the benefits that consumer involve-

ment can bring to the scope, validity and acceptability of research. The session was followed by a lively panel discussion which included Professor Phyllis Butow. Questions from the floor ranged from how best to access consumer representatives, to how consumer representatives might add to all levels of research.

THE ANZ Gynaecological Oncology Group ASM 2015 and the ANZGOG New Research Fund

The *Contemporary Management of Gynaecological Cancer* was the focus of the ANZ Gynaecological Oncology Group's (ANZGOG) Annual Scientific Meeting 2015, held on 25 – 28 March on the Gold Coast. Over 170 medical oncologists, gynaecological oncologists, radiation oncologists, cancer researchers, study coordinators, nurses and consumers came together from across Australia and New Zealand to consider the current trends in research and treatment of gynaecological cancers.



International keynote speakers, Dr Keiichi Fujiwara, Gynaecological Oncologist from Saitama Medical University and Professor Charlie Gourley (pictured), Medical Oncologist from

Edinburgh gave well received presentations on the management of ovarian cancer.

This year's conference also had an overall celebratory atmosphere as ANZGOG marked 15 years of amazing achievement and success. ANZGOG has much to be proud of including \$14 million worth of research grants, 19 clinical trials, over 3000 patients recruited and a membership of 650 multidisciplinary members.

The next ANZGOG Annual Scientific Meeting will be held in Sydney from 13-16 April 2016. The convenor of the conference is Associate Professor Peter Sykes.

ANZGOG has also recently established a New Research Fund grant program to promote the development of investigator studies from initial concept to full study. \$100,000 has been set aside in 2015 to support up to four projects which may be:

1. A young or new investigator's study.
2. Innovative sub-studies.
3. Pilot studies (including generating data to support preparation for a larger research pro-

4. Seed funding for a high priority ANZGOG study.

The research project submitted must first be approved by the Research Advisory Committee as an ANZGOG study and have direct alignment with ANZGOG's research priorities as defined in the Five Year Strategic Plan and by the Board of Directors.

Applications from ANZGOG members only open 1st July and close 31st August. For more information about the New Research Fund Grants, email Alison Evans, ANZGOG Executive Officer at alison.evans@anzgog.org.au



ANZGOG ASM, 2015

Guidance on Conducting Economic Evaluations Alongside Clinical Trials

One of the key challenges in undertaking economic evaluations is how to best source the data required to estimate resource use (costs) and outcomes. Broadly, there are two avenues for collecting such information – directly from a clinical study, or from existing published sources. Collecting such data from clinical trials is one way to ensure that it is relevant to the clinical question being investigated, potentially reflects local clinical practice, and directly captures patient relevant experiences. However, designing economic evaluations alongside clinical trials can be complex and requires an expansion of the study design phase. The International Society for

Pharmacoeconomics and Outcomes Research (ISPOR) recently published an update to its guidance on practices to follow when conducting an economic evaluation alongside a clinical trial.

The recommendations cover all critical aspects including thinking about the trial design, data collection, how the data might be analysed, and subsequently reported. An overview of the key inputs and issues to consider are provided below, with the full reference available via: <http://www.sciencedirect.com/science/article/pii/S1098301515000169>

Considerations	Issues to Support Economic Evaluation
Trial Design	
Appropriateness of trial design	Study should reflect pragmatic effectiveness, rather than efficacy. Trial should be generalisable in its approach.
Threats to external validity and generalisability	Protocol driven resource use. Inappropriate (uncommon/unused) comparators. Non-representative recruitment. Restrictive participation criteria. Artificially enhanced compliance.
Sample size and power	Typically powered on clinical issues, underpowered for economic analysis. If powering on an economic endpoint, the stated cost-effectiveness threshold should be included.
Study end-point and comparator	Present clinical endpoints in a disaggregated form to facilitate an economic evaluation. Value endpoints using utility weights (to produce quality adjusted life years; QALYs) or money (for a cost-benefit analysis). Avoid intermediate or surrogate outcomes if possible.
Appropriate follow-up	Consider the relationship between the within trial and longer term health care use and quality of life. Data collection should be sufficiently frequent to capture the impact of treatment on expected changes in resource consumption and quality of life, without adding to trial burden. Include baseline data to allow for any necessary between group adjustments to be made.
Data Elements	
Pre-trial value of information studies	Use of value of information and modelling studies pre-trial can guide which resource use and patient level outcomes data are expected to be the drivers of costs/outcomes.
Patient-level data: resource use	Prioritise data collection for high cost inputs, or those expected to differ between treatments. Too narrow a perspective on cost collection might be a missed opportunity as treatments might have unintended consequences and trials are unlikely to be repeated. Frequency and media for resource use collection should be aligned with clinical measures, but depends on the availability of electronic data records. Where possible use validated instruments for resource use and productivity data collection; validate with secondary data sources.

Guidance on Conducting Economic Evaluations Alongside Clinical Trials (cont.)

Considerations	Issues to Support Economic Evaluation
Patient-level data: preference based outcomes	<p>Apply preference based health state classification systems (eg. EQ-5D, AQoL-8D, SF-6D derived from SF-36) directly to patients.</p> <p>Timing depends on expected treatment effects.</p> <p>Including generic and disease specific instruments might be appropriate to allow for scenario analyses.</p> <p>Direct preference studies, such as time-trade-off, standard gamble or discrete choice experiments, might be appropriate where process of care affects quality of life.</p>
Patient-level data: Data/Collection Tracking	<p>Electronic tracking/entry in “real-time” allows data to be collected closer to clinical events.</p> <p>Needs to be validated against traditional data collection methods.</p>
Institutional data	<p>Collect provider, site-level or country level data on practice patterns to assess generalisability of study data.</p>
Valuation of re-sources	<p>Consider impact of different coding systems, timing and potentially currencies in applying costs to resource use.</p>
Database Design and Management	
Data entry and collection	<p>Early and regular monitoring of resource use and preferences data.</p>
Informed consent	<p>Ensure consent covers collection of resource use and preferences data.</p>
Confidentiality and modelling	<p>Consider whether post-trial availability of patient level data for modelling and meta-analyses will compromise patient confidentiality.</p>
Analysis	
Guiding principles	<p>Prepare an analysis plan for the economic evaluation prior to trial unblinding. Common elements include:</p> <ol style="list-style-type: none"> 1. ITT approach 2. Common time horizon for analysis of costs and outcomes (within trial or extrapolated). 3. Report measures of uncertainty (standard errors, p-values, confidence intervals as appropriate). 4. Apply discounting if appropriate. 5. Consistent approach to missing data.
Trial costs	<p>Estimate overall costs, and simple arithmetic mean cost differences for treatment groups.</p> <p>Comparisons using bootstrapping to account for the non-parametric nature of the data.</p> <p>Cost modelling might be required to account for differences in patterns of resource use, including specifying disease related treatment costs.</p>
Trial outcomes	<p>Where possible use the same method of analysis as in the trial.</p> <p>Composite clinical endpoints need to be translated for use as economic endpoints; the linkage needs to be clearly stated.</p> <p>Construction of QALYs should be clearly stated, and carried out using area-under-the-curve methods.</p> <p>Where outcomes are not statistically different a cost-minimisation analysis should be performed.</p>
Missing and censored data	<p>Determine the nature of the missing and/or censored data, and how it will be treated.</p> <p>Dropping cases with missing data is not recommended due to the potential for inducing bias. Potentially ignore missing data if frequency is low (<5%) and has the same pattern across treatment groups.</p> <p>Consider multiple imputation methods for dealing with extensive missing data.</p>
Summary measures	<p>Consider how comparative costs and outcomes will be expressed:</p> <ol style="list-style-type: none"> 1. Ratio measure: incremental cost over incremental benefits; 2. Difference measure: use of common metric (typically money), and take difference of costs and benefits; and 3. Probability measure: likelihood a treatment will be cost-effective based on the incremental costs and benefits.

Guidance on Conducting Economic Evaluations Alongside Clinical Trials (cont.)

Considerations	Issues to Support Economic Evaluation
Uncertainty	Test sampling uncertainty by deriving confidence intervals around the ICER, or acceptability curves (probability measure). Value of information analyses can be used to estimate willingness to pay to reduce uncertainty associated with cost-effectiveness. Conduct sensitivity analyses around parameter estimates (inputs) for costs and outcomes. Test sensitivity of results to imputation methods using bootstrapping techniques.
Country specific costs for multinational studies	Test generalisability of multinational study results to a country of interest: <ol style="list-style-type: none"> 1. Test homogeneity of results (outcomes and resource use) across countries; 2. Multivariable cost and outcome regressions to adjust for country effects; and 3. Multilevel random effects modelling with shrinkage estimators.
Including Costs and Effects beyond the time horizon of the trial	Extrapolate (project) costs and benefits over the expected duration of treatment and its effects. Follow good-modelling practices. Estimate cost-effectiveness ratios at different time points to inform decision making and summarise trajectory of outcomes.
Subgroup analyses	Should be pre-specified to avoid spurious findings.
Reporting	
Consolidated Health Economic Evaluation Reporting Standards (CHEERS)	Reporting of results should follow the CHEER statement: <ol style="list-style-type: none"> 1. Description of trial issues and findings 2. Data collected for the economic study 3. Methods of analysis 4. Results of the economic analysis

Workshop on Quality of Life and Utility Measures in Cancer Research

Save the Date: Friday 14th August 2015

Workshop on quality of life and utility measures in cancer research

Facilitated by: the QoL Office and CREST

Level 5 Education Centre, Chris O'Brien Lifehouse, Camperdown NSW 2050

The workshop is free to members of any of the 13 Australia and New Zealand Cancer Clinical Trials Groups. A formal call for registration will be made through the QoL Office in the coming weeks, along with information about applying for limited travel support. For any queries please contact Dr Claudia Rutherford:

claudia.rutherford@sydney.edu.au



COGNO
COOPERATIVE TRIALS GROUP
FOR NEURO-ONCOLOGY

8th COGNO Annual Scientific Meeting
'Where the Future Lies'
Friday 23rd – Saturday 24th October 2015
Stamford Plaza Brisbane, Queensland, Australia

NHMRC Clinical Trials Centre 

COGNO ASM Update

With so much focus on glioblastoma research in an attempt to improve patient outcomes, sometimes it's easy to overlook grade II and III gliomas. But with long-term follow-up data now published in both these tumour grades, practices may be changing.

Come and join us for Session 2: *Grade II and III Glioma: The present and the future* and hear two of our four confirmed international guests, [Martin van den Bent's](#) and [Kenneth Aldape's](#) perspectives on the changing landscape of these tumours.

[Click here](#) to view the preliminary program.

Take advantage of the Early Bird rates and [register now](#).

Don't forget to [submit your abstract](#).

Important Dates

Early Bird Registration Closes	31 July 2015
Abstract Submission Deadline	31 July 2015
EOI for Sponsored Foreign Delegate Attendance Submission Deadline	31 July 2015
Sponsored Foreign Delegate Attendance Recipient Notified	28 Aug 2015
COGNO/CINSW Travel Grant Submission Deadline	4 Sep 2015
Abstract Presenters Notified	Sep 2015
COGNO/CINSW Travel Grant Recipient Notified	Sep 2015
Deadline for Abstract Presenters to Register	25 Sep 2015
Online Registration Closes	9 Oct 2015
COGNO Annual Scientific Meeting	23-24 Oct 2015

See you in Brisbane!

Dr Cecelia Gzell
Radiation Oncologist
8th COGNO ASM Convenor

W: www.cogno.org.au

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What's CREST Been Up To?

Trial Group Collaborations:

Attendance and participation at the COGNO Ideas Generation Workshop in Sydney (27th March 2015).

Attendance and participation at the GCCTI Industry Workshop in Sydney (10th April 2015).

Presentation to the Executive Officers Network in Sydney (21st April 2015).

Presentation to the Joint CANTEEN and ANZCHOG National Patient and Carer Advisory Group in Melbourne (8th May 2015).

Attendance and participation at the PoCoG Concept Development Workshop in Sydney (13th May 2015).

Presentation at the ANZCHOG Young Researchers Grant Writing Symposium

in Sydney (28th May 2015).

Other Activities:

Ongoing meetings with the Clinical Trial Group Executive Officers.

Trial protocol and data collection advice.