

## Evaluation Alongside a Clinical Trial?



Thinking about how best to incorporate economic evaluations alongside clinical trials is one of the core services provided at CREST. A recent review by Hughes et al (2016) in *PharmacoEconomics* provides a very useful summary of the key questions to consider when thinking about conducting an economic evaluation alongside a clinical trial; from whether or not an evaluation is required, to how best to handle missing data – it's all there! Here we provide a precis of the key points from that review.

There are various reasons to undertake an economic evaluation. It might be that an intervention seems likely to produce a *different therapeutic benefit* or to involve *different costs* than its comparator, or there is *uncertainty* around the cost-effectiveness of an intervention or its *budget impact* is anticipated to be high. RCTs might not always be the best way to collect the evidence required to answer those questions. Sometimes, decisions about implementation need to be made before trial results are available. Also, trials may include comparators that differ from routine care or

include selective subpopulations of patients. In these circumstances, it might be preferable to conduct an economic evaluation using a decision analytic model using existing data.

In many cases though, it is preferable to conduct an economic evaluation alongside a clinical trial. This includes cases where costs are largely driven by the primary outcome of the trial, where considerable heterogeneity of costs is expected, or where adherence to the intervention may drive costs and outcomes. Whether a particular trial is a suitable vehicle for an economic evaluation depends on its *design*, whether *current practice* is one of the alternatives being compared, and if the trial *setting* provides generalisable results. Ideally, trials must be at least partly pragmatic (relating to actual clinical practice) if they are to be suitable for economic analysis.

Various methods exist to collect resource use information in a trial-based economic evaluation. These include using data from routine medical records, data collected for the purposes of payment, data collected within case report forms, and/or data from patient questionnaires. In case of the latter, it is important to realise that data which rely on patient recall are

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## Thinking About an Economic Evaluation Alongside a Clinical Trial (cont.)?

subject to bias, which may adversely affect the resulting cost estimates. When contemplating the use of routinely collected data, issues to consider include the cost of obtaining the data, the delay between a patient exiting the trial and the data becoming available, the potential for missing data, and the complexity of data management. Useful Australian sources of routinely collected data are the Medicare data (pharmaceutical via the PBS and medical/diagnostic service use through the MBS see: <http://www.crest.uts.edu.au/pdfs/Factsheet-Medicare-Australia-UpdatedNov2015.pdf>), linked data (e.g. Admitted Patients Data Collection for some states, such as are available through the [CHEREL](#) for NSW) and cancer registries.

A common issue for trial-based economic evaluations is that trial follow-up periods are typically too short to capture all differences in health effects and resource use. In this case, data modelling techniques are needed to extrapolate trial results beyond the observed period. Typically, a trial based analysis is complemented by a model based analysis, potentially informed by data from one or more sources outside of the clinical study. Another potential issue is missing data which can result in a loss of precision and statistical power, which may bias the results of an economic evaluation. Possible solutions are to minimise the potential for missing data at the trial design stage, use multiple sources of data which can complement each other, and impute missing data where appropriate.

Generalisability is a key issue; does the intervention which worked in the trial work just as well in clinical practice? That is, does the efficacy observed in the trial translate into clinical effectiveness? Differences in trial-based efficacy and practice-based effectiveness arise due to clinical and

other differences between the patients included in trials and those treated in practice, and the procedures mandated in trials relative to “real-world” clinical practice. Another key area to consider is the effect of non-adherence. Failure to consider the possibility of differences in adherence between the trial and clinical practice in economic evaluations can lead to biased estimates of cost-effectiveness. A variety of modelling methods exist which enable data to be adjusted to account for non-adherence including conventional or decision analytic approaches, discrete event simulation and mechanism-based modelling.

Finally, Hughes et al (2016) highlight that economic evaluations alongside trials may be challenging where they involve the synthesis of data from multiple centres across different countries. Costs of care can vary widely from one country to another, some of which is due to differences in price weights and clinical practice. Furthermore, care needs to be taken in applying outcome measures to different countries, particularly where local preference based measures have been used.

Conducting an economic evaluation alongside a clinical trial can be a powerful means of addressing important questions on the comparative value of a new intervention. Keeping in mind the points from this review by Hughes et al (2016) will help to ensure that the collection and analysis of the data can indeed be used to answer those questions in a manner that is meaningful to the researcher and health care decision makers alike.

1. Hughes et al. (2016) “Conducting Economic Evaluations Alongside Randomised Trials: Current Methodological Issues and Novel Approaches”, *Pharmacoeconomics* 34:447-461.

*Contributed by N van der Linden*

## ANZBCTG Annual Scientific Meeting

Registration is open for the Australia and New Zealand Breast Cancer Trials Group's (ANZBCTG) joint Annual Scientific Meeting (ASM) with the Clinical Oncology Society of Australia (COSA) from 15-17<sup>th</sup> November 2016.

The conference will be held at the Gold Coast Convention and Exhibition Centre and is an opportunity for members of both organisations to share knowledge in the field of breast cancer research and to develop these important relationships between research and medical professionals.

The program will include three days of presentations and international speakers include:

Dr Laura Esserman, Professor of Surgery and Radiology at the University of California, San Francisco (UCSF), and the Director of the UCSF Carol Franc Buck Breast Care Centre.

Dr Deborah Fenlon, Associate Professor in the Faculty of Health Science, University of Southampton, UK.

Dr Shom Goel, Physician-Scientist at the Dana-Farber Cancer Institute and Harvard Medical School in Boston USA.

Dr Jay R Harris, Dana-Farber Cancer Institute USA.

Dr Melinda Irwin, Professor of Epidemiology in the Yale School of Public Health, Deputy Director of Public Health for the Yale Center for Clinical Investigation USA.

Applications for ANZBCTG Awards, including Avon Travel Grants, are open and will close on 11 July 2016. To view the range of awards available and the eligibility criteria, visit the ANZBCTG website at [www.anzbctg.org](http://www.anzbctg.org).

The conference website and registration pages are available at [www.cosa2016.org](http://www.cosa2016.org). We look forward to seeing you there!



*Contributed by: Anna Fitzgerald, ANZBCTG.*

### ***Do you have a trials group newsletter?***

***CREST can provide articles which introduce CREST services, or which provide commentary on a health economics topic of interest to your members.***

***Please contact us if you would like to discuss the possibilities.***

## Real-World Data in Oncology

“Real-world data are key to improve the quality and cost-effectiveness of cancer care”. Thus concludes Dr Naomi van der Linden in her PhD thesis on the importance of patient registry data in evaluating the clinical and cost-effectiveness of oncology treatments.

New oncology treatments are studied extensively before they are approved for marketing. Typically, the safety and efficacy of treatments is demonstrated through clinical trials. However, after entering the market, important questions remain about real-world clinical use, safety and cost-effectiveness of treatments in clinical practice as distinct from the clinical trial setting.

In particular, the cost-effectiveness of treatments in clinical practice may differ substantially from that estimated based on trial results. This arises due to differences in the characteristics of patient populations in trials and clinical practice, and health care practices. Naomi explored this question in her PhD, focusing on the treatment of lung cancer and head and neck cancer. A key aspect of her methods was to develop a patient registry for the collection of clinical and resource use data associated with the treatment of those patients. These registry data were used to supplement trial evidence to determine the cost-effectiveness of treatments within those settings in clinical practice. Through her research, Naomi showed how trial evidence and registry data can be combined in decision analytic models to obtain more realis-

tic estimates of cost-effectiveness with which to inform decisions about resource allocation.

In her thesis, Naomi showcases a variety of studies performed using real-world data, including evaluation of the cost-effectiveness of cetuximab in the setting of head and neck cancer. Throughout her work, she explores the advantages and disadvantages that using such data brings, and provides practical guidance in setting up patient registries to inform healthcare decision making. Expect more on this in future publications.

Naomi completed her PhD at Erasmus University in the Netherlands in 2015, and is now a Research Fellow with the Centre for Health Economics Research and Evaluation at UTS.



Dr Naomi van der Linden

## What Influences the Quality of Life Following Paediatric Cancers: Comparing Survivors and Parents-of-Survivors.

A recent commentary in the JNCI highlighted the effects of chronic conditions on quality of life (QoL) among survivors of paediatric cancers.<sup>1</sup> Using the SF-6D, an utility based measure of QoL, Yeh et al (2016) demonstrated that having multiple and severe chronic health conditions reduced QoL in survivors of paediatric cancers.<sup>1</sup> Comorbid conditions, among other factors, were also identified as affecting QoL in survivors of paediatric cancers in Australia in a recently completed study by Ramon Tillemans.

As you might recall from an earlier newsletter, Ramon was a Masters student who undertook a project jointly supervised by the team at CHERE and the Behavioural Sciences Unit, Kids Cancer Centre, Randwick. Working with data collected as part of the Long-Term Follow-Up Study, Ramon sought to understand the factors influencing the QoL of 470 paediatric cancer survivors and parents of paediatric cancer survivors. Survivors of paediatric cancers aged over 16

years, or the parents of those aged under 16 years, who had completed treatment more than five years prior and who agreed to participate in the study, provided information on socio-demographic and clinical characteristics, as well as QoL. QoL among survivors and parents was assessed using the EQ-5D-5L, with an additional measure of survivor's QoL provided by parents using the KIDSCREEN-10.

Using univariate and multivariate analyses, Ramon showed that for the 317 paediatric survivors and 153 parents, the main QoL domains affected were pain/discomfort, and anxiety/depression. Both survivor and parent QoL were heavily influenced by their respective current health status, but differed with respect to the influence of other factors. Survivor QoL was affected by a number of factors including prior therapies received, the presence of comorbidities, and their use of financial support. In contrast parents' QoL was affected by pri-

vate health insurance status, and their child's QoL rating according to the KIDSCREEN-10.

Overall, through this project Ramon has demonstrated some important similarities and differences about the factors that influence QoL in longer-term survivors of paediatric cancers and the parents of survivors. Data from this study, the brainchild of the Behavioural Sciences Unit, Kids Cancer Centre, Randwick - proudly supported by the Kids with Cancer Foundation, and The Kids Cancer Alliance (<http://www.behaviouralsciencesunit.org>) - will continue to accumulate allowing further opportunities to investigate outcomes among survivors of paediatric cancers. In the meantime, look out for publications of the full results from the current analysis.

1. Yeh JM, Hanmer J, Ward ZJ, et al. Chronic Conditions and Utility-Based Health-Related Quality of Life in Adult Childhood Cancer Survivors. *J Natl Cancer Inst* 2016; 108.

## Quality of Life and Utility Measures in Cancer Research – A Workshop

24<sup>th</sup> August 2016

In conjunction with the Asia-Pacific Chapter of ISPOR, the Quality of Life Office and CREST will be presenting a workshop in August 2016.

This workshop will:

Explain the rationale for assessing HRQOL/PROs in clinical studies and for economic evaluation

Introduce QALYs and utilities

Explain methods of measuring and valuing HRQOL, and how these differ

Introduce the new cancer-specific utility instrument – the QLU-C10D (derived from the QLQ-C30)

The workshop and following networking function are being held on Wednesday, 24<sup>th</sup> August 2016, from 9 am to 5:30 pm at UTS, Sydney. Attendance at the workshop is subject to a registration fee, with discounts for ISPOR members. For full details and to register please visit: [www.isporac.org/events/qolwks](http://www.isporac.org/events/qolwks)

## What has CREST been up to?

### Trial Group Collaborations:

- Participation in the ANZUP Concept Development Workshops, Sydney, May 2016.
- Participation in the COGNO Ideas Generation Workshop, Sydney, May 2016.
- Participation at the GCCTI Workshop 4, Melbourne, April 2016
- Ongoing advice on the development of trial protocols and data collection forms.

### Workshops:

- TCRN/Catalyst, Economic Evaluation in Implementation Science, April 2016
- CREST, Understanding Health Economics for Cancer Clinical Trials, UTS, April 2016
- Presentation at the QoL Office, Protocol Workshop, May 2016.

### Other Activities:

- Continuation of the Structured Training Opportunities program.
- Authorship on a publication in Oncology Therapy: LT Bloem, R De Abreu Lourenço, M Chin, B Ly, M Haas, “Factors Impacting Treatment Choice in the First-Line Treatment of Colorectal Cancer”, Oncology Therapy, pp 1-4, doi: 10.1007/s40487-016-0020-4