Including Patient Preferences in Clinical Trials through Discrete Choice Experiments

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. Typically, economic evaluations focus on health outcomes measured as quality adjusted life years (QALYs), and the incremental costs associated with producing those outcomes. But it is not always the case that health is the only outcome of interest; for some interventions non-health outcomes such as convenience, continuity of care, trust and satisfaction with care might also be of interest. Discrete choice experiments (DCEs) are widely used in health economics to measure the value attached to both health and non-health outcomes. DCEs ask participants to choose between alternative interventions in a survey based experiment, thereby demonstrating the value they place on the characteristics, or attributes, used to describe those interventions. The preferences expressed in this way can be used to derive quality of life values for use in estimating QALYs or, more commonly, the respondents’ willingness to pay (WTP) for the attributes of the interventions of interest. Thus DCEs can be used to inform cost-utility analyses, through the estimation of QALYs, and cost-benefit analyses (CBA), through the estimation of WTP.

In a recently published study, Tinelli et al. (2016) note that while many DCE studies have generated monetary values using WTP, the application of these values within a subsequent economic evaluation has rarely been considered. The authors build on an RCT previously conducted in the UK, and conduct a DCE 12 months later among the original trial participants to assess their preferences for the treatment attributes and their associated WTP. The resulting WTP values were used to inform a CBA which was compared with the results from a prior cost-per-QALY analysis.

The DCE and subsequent CBA were conducted following the Medman Trial, a multi-centre study investigating a new model of collaborative pharmacy medicine services in patients with coronary heart disease. The study considered changes in appropriate treatment use, health outcome risks, patient satisfaction and costs arising from a more coordinated medicine review compared with current practice. These aspects of the trial, as well as inputs from a satisfaction survey conducted at the end of the RCT and from prior pharmacy research, were subsequently used to determine the attributes included in the DCE (see an example choice set is provided at Figure 1). Crucially, a ‘cost’ (price proxy) attribute was included so that respondents’ willingness to pay (WTP) could be estimated.

The published paper highlights key methodological issues to consider when incorporating a DCE into a clinical trial to inform an economic evaluation, including: (1) What attributes need to be addressed - the attributes and levels for the DCE should at least be informed by the aim of the trial itself; (2) Whose preferences should be assessed within the trial - it could be assumed that...
patients in the trial with direct experience of the intervention will value it more than those who have no experience of it; and (3) When they should be valued – assessing preferences at trial completion might only capture those with an existing preference for an intervention, particularly if there were opportunities for earlier discontinuation (patients no longer receiving the intervention might value it less).

As noted above, the intention of incorporating the DCE as part of the Medman trial was to conduct a CBA within the trial population and to compare its results with those from a cost-per-QALY analysis. The results of the cost-utility analysis showed no statistically significant differences in terms of costs, appropriate treatment scores or QALYs. In contrast, the results of the CBA showed a difference between the intervention and control groups; patients with experience of the service had a positive WTP and those in the control group a negative WTP. Within the intervention group, those who continued voluntarily with the intervention after the trial ended had the strongest WTP for the pharmacy consultancy service, while those that discontinued did not value the service.

A similar pattern of benefit was observed using the net benefit calculations, defined as the WTP (from the DCE) minus the difference in societal costs reported from the analysis of the Medman trial.

Tinelli et al. (2016) note that including a DCE alongside a clinical trial provides values of increased (or decreased) satisfaction with an intervention that are consistent with the current literature – and therefore suggest that it is possible to elicit a value for process effects associated with patient care. Incorporating those values into an economic evaluation, in this case by using WTP values derived from the DCE, can result in conclusions that differ from a cost-per-QALY analysis. Including patient preferences in this way can thus be used to inform policy decisions regarding the delivery of health-care services.

Figure 1: An example choice set


Contributed by Martin Flattery

Genomic Cancer Clinical Trials Initiative September 2016 Workshop: Opportunity to Contribute

The aim of the Genomic Cancer Clinical Trials Initiative (GCCTI) is to support Australia’s cancer clinical researchers to develop mutation-specific clinical trial concepts and grant applications involving cancers from more than one primary site and more than one of the national cancer cooperative trials groups (CTGs).

The GCCTI project team in collaboration with the Scientific Steering Group will host an all-day workshop on Friday, 30 September in Sydney. This workshop has been set-out to discuss and develop new concepts for grant applications. Please feel free to submit potential ideas/concepts that you think may be relevant to GCCTI. An idea generation template is available on the GCCTI website. Please submit your ideas/concepts for discussion at the upcoming workshop to Nicci Bartley at nicci.bartley@zest.com.au before Friday, 16 September.

Do not hesitate to contact Nicci Bartley if you have any questions.

Contributed by Nicci Bartley
Patient-reported outcomes provide information about the impact of disease and treatment on the patient, and PROs can be interpreted in the context of other trial outcomes to provide a comprehensive assessment of treatment benefits and harms. PRO studies often suffer from missing data, which, if not handled appropriately, can cause major problems for analysis and interpretation. Missing data can be caused by issues related to the patient’s illness (e.g. when patients die or are taken off trial due to disease progression), or for reasons unrelated to the patient’s illness (e.g. administrative errors). Some types of missing PRO data are preventable. In other cases, the potential for missing PRO data to lead to bias may be reduced by thoughtful design, implementation and reporting strategies.

The QOL Office recently published a systematic review collating practical strategies to minimise the problem of missing PRO data, from over 117 sources. The review highlights that potential issues with missing PRO data need to be considered from the trial design stage through to the reporting stage by all members of the trial team. The review paper is available open access online: http://bmjopen.bmj.com/content/6/6/e010938

If you would like assistance with a missing PRO data concern, please contact the QOL Office: https://sydneypsy.qualtrics.com/SE/?SID=SV_eV85Bh9eW84R0In

Contributed by Rebecca Mercieca-Bebber

Joint ANZBCTG/COSA Annual Scientific Meeting

The Australia and New Zealand Breast Cancer Trials Group’s (ANZBCTG) joint Annual Scientific Meeting with the Clinical Oncology Society of Australia (COSA) will be held from 15-17 November 2016, at the Gold Coast Convention and Exhibition Centre. The conference is an opportunity to share knowledge in the field of breast cancer research and to develop these important relationships between research and medical professionals.

An audience of 1,200 delegates is expected and the program includes plenaries and concurrent sessions with invited speakers and proffered papers, co-badged trade sessions, company organised symposia, poster presentations, workshops and several networking events. The full conference program and registration pages are available at www.cosa2016.org.

Contributed by Anna Fitzgerald
## Around the world, assessing value for money in terms of the cost per quality adjusted life year gained using cost-utility analysis (CUA) is becoming increasingly important for decision making in allocating public health care expenditure. The use of CUA is preferred by reimbursement bodies in a number of countries including the UK, Canada and Australia.

An integral part of using CUA to inform reimbursement decisions is the quality of the studies used to derive that evidence. A recent systematic review by Nerich et al. (2016) published in *Breast Cancer Research and Treatment* aimed to identify and critically appraise the quality of published CUA studies in breast cancer diagnosis and therapy. The studies reviewed covered a broad range of breast cancer related therapies including: drug therapies for breast cancer (chemotherapy, hormonotherapy, and targeted therapies); drug therapies for the prevention and/or treatment of side effects associated with breast cancer treatment; drug therapies for clinical complications of breast cancer; gene expression profiling to guide adjuvant treatment decisions; and testing of HER2 status to determine eligibility for trastuzumab.

From a citation list of 2,739 articles identified from the electronic search, a total of 140 articles were included in the systematic review and reviewed according to the CHEERS checklist and the Drummond checklist for review of published evaluations. The review showed that since 2000, the majority of CUAs were published in the period 2009-2011 (n=47, 34%), with the majority appearing in clinical journals (n=110, 79%). The most common stage investigated was early stage breast cancer (n = 102; 73 %), and most often in the adjuvant treatment setting (n = 101; 72 %). Drugs for breast cancer were the technology most widely investigated in the published CUAs (see Figure 1). A quarter of the published CUAs took the perspective of the US (n=35, 25%), followed by the UK (n=25, 18%) and Canada (n=24, 17%), with the remainder coming from multiple countries. The health care system perspective was adopted most commonly (n=110, 79%) across studies, with relatively few (n=19, 14%) adopting a societal perspective in their analysis.

Overall the quality of the published studies was high; over half (n=74) of the included papers achieved a quality score ≥ 7 (out of 10). However, Nerich et al. (2016) noted that quality was compromised for many of the published CUAs in terms of presenting only partial sensitivity analyses (they did not assess the robustness of their results to shifts in all the relevant parameters), limited discussion of the results, the valuation of costs and consequences, and the identification, measurement, valuation and use of utility values to assess quality of life.

Nerich et al. (2016) also investigated the factors associated with being classified as a high quality CUA. Three factors were shown to be significantly associated with increasing the likelihood of being rated as a high quality CUA: when first authors were employed by a consulting or pharmaceutical company; when the study investigated gene expression profiling; and when both a cost-utility and cost-effectiveness analysis (such as the cost per life year) was presented.

This review highlighted that while there has been an increase in the number of CUAs for breast cancer over time, particularly for drug therapies, there remains scope to improve the quality of those studies. The authors conclude that there is a need for better adherence to international guidance on the conduct and reporting of CUAs to improve their overall quality and comparability.

### Figure 1. Technologies Investigated in CUA Studies


*Contributed by S Saing*
ANZMTG Update

Australia has the highest incidence of melanoma in the world and it is often referred to as Australia’s national cancer. The Australia and New Zealand Melanoma Trials Group (ANZMTG) co-ordinates and conducts quality research within the field of melanoma, conducting both national and international Investigator led trials. Our free membership is currently composed of over 1,100 members, across 30 countries and from a diverse range of backgrounds including research, health care and melanoma support networks.

ANZMTG’s clinical trial portfolio and collaborator base is growing at a pace that is quickly beginning to match the rapid advancements made in new melanoma treatments and technology. Our current trials cover a broad spectrum of treatments for melanoma. All of our trials have the same aim of ensuring better prevention, treatment and care of current and future melanoma patients.

ANZMTG has also experienced increased participation from an increasing number of national and international collaborators, with our trials currently active in more than 14 countries worldwide.

The research output of ANZMTG reflects the diligence of the team and the dedication of the various collaborators and investigators we work with and has led to the increasingly rapid growth of the group. This level of commitment and hard work has instilled dynamism in the team and has allowed us to work effectively toward the goal of establishing scientifically rigorous, clinically relevant trials which will generate much needed evidence to guide care for melanoma patients.

ANZMTG works closely with CREST to embed health economic components within our trial designs; with the aim of generating appropriate data to evaluate the cost-effectiveness of our treatment interventions in each protocol.

The 2016 ANZMTG Annual Meeting was held in Melbourne on Friday the 26th of August as part of the Inaugural Locoregional Melanoma 2016. During the meeting ANZMTG current and future trials were presented along with an update on the growth and future direction of the group. Meeting materials including our 2016 yearly report are available on our website www.anzmtg.org

Please contact anzmtg@melanoma.org.au for more information.

Contributed by Alex Economides

CREST and ANZUP

Throughout the year, members of CREST have participated in numerous ANZUP events on the design of clinical trial concepts, informing consumers and engaging with the broader public. The team has participated in the four tumour stream specific concept development workshops held so far this year: prostate cancer, germ cell tumours, bladder cancer and renal cell carcinoma.

In addition, they have provided ad-hoc advice during the tumour stream sub-committee teleconferences. In July, Richard from CREST attended the 2016 ANZUP ASM where he presented to the ANZUP Consumer Advisory Panel on the role of health economics in clinical trials, participated in the “Community Engagement Forum - A Little Below the Belt” with members of the public on the benefits of clinical trials in supporting treatment funding and access, and attended the concept development session for new trial ideas. These sessions and engagement with ANZUP not only help increase awareness of the importance of health economics in informing clinical trials in this setting, but are an important sharing of information that helps to build better advice.

Discussion from the floor during ANZUP ASM 2016.
Come join us for an outstanding Scientific Program!

The 9 sessions include; ASNO Country Updates, New molecular classification of glioma, Managing imaging and recurrence, Next generation clinical trials, Translational research, #Quality of life: the digital era, All things Allied Health, Technology advances on the horizon, and State of the art – Immunooncology. Click here to view the program.

Expert International and Asian guest faculty include; Paul Mischel, Mitch Berger, Roger Stupp, Sona Pungavkar, Arjun Sahgal, Al Yung, Greg Riggins, Rakesh Jalali, Mary Lovely, Don Berry, Brian Alexander, Tim Cloughesy, Fabio Iwamoto and Anna Barker. Click here to learn more about the Keynote and Invited Speakers.

Combined with a stellar line-up of Oral Abstract presentations - and delegates from diverse countries and craft groups - the 2016 ASNO-COGNO sessions promise exciting new conversations and collaborations.

On Sunday 11 September we will be hosting two workshops:

SRS Workshop, 0845 to 1700; An interactive and informative workshop where participants will hear from international experts about the different technologies, techniques, applications and appropriate uses across a range of benign and malignant tumours; from benign base of skull lesions, pituitary tumours, to brain metastases.

Glioma Master Class, 1300 to 1700; A unique opportunity for participants to hear how our panel of acclaimed international and national speakers care for their patients: “How I do it”.

Click here to view further information on the workshops.

A number of additional meetings are available on Monday to Wednesday:

CNS Lymphoma Lunch Symposium
Monday 12 September - 1200 to 1300

Difficult Dialogues Lunch Symposium
Tuesday 13 September - 1230 to 1330

GBM AGILE Meeting
Wednesday 14 September - 1315 to 1415

Click here for further information on the additional meetings.

Onsite registration will be available, click here for further information.

We look forward to hosting you in Sydney!

Contributed by Yi Feng

What has CREST been up to?

Trial Group Collaborations:
- Participation in the ANZUP Concept Development Workshops and ASM.
- Participation at the PoCoG Concept Workshop, Sydney, June.
- Ongoing advice on the development of trial protocols and data collection forms.

Workshops:
- ISPOR NZ and NZACRes Workshop on Health Economics in Clinical Trials, Auckland.
- ISPOR AP, QoL Office joint industry workshop on QoL and Utility Measurement.

Other Activities:
- Presented at the KCA Cancer Pre-disposition Symposium. (26th August).
- Ongoing research involvement and structured training opportunities.