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CREST Update—Mar 2015

Introducing the QLU-C10D: a Utility Measure based on the QLQ-C30.

The EORTC QLQ-C30 is one of the most commonly used quality of life (QoL) measures in cancer clinical trials internationally, so will be familiar to many members of the Co-operative Clinical trials groups. It contains 30 questions assessing common cancer symptoms, functioning and global QoL. It therefore provides a comprehensive assessment of patient-reported outcomes (PROs) that are important to patients and their health care providers. However, as originally designed, the QLQ-C30 cannot be used in health economic analysis because it is not a preference-based measure (or utility measure).

The most common utility measures are the EQ-5D, HUI3 and SF-6D. Although these measures are widely used, they are generic, and therefore may not be particularly sensitive when used in cancer populations. Furthermore, the use of several questionnaires (e.g. QLQ-C30 for QoL endpoints and EQ-5D for health economics) adds to PRO completion time and patient burden.

An international team led by Professor Madeleine King (of Cancer Australia's Quality of Life Technical Services) and Professor Rosalie Viney (of CREST) has spent the last 4 years, developing a utility measure from the QLQ-C30. The project is funded by an NHMRC project grant. The new measure is called the QLU-C10D: 'QLU' indicates it is a utility measure; 'C' indicates its origin in the EORTC's core questionnaire; and '10D' indicates 10 domains (mobility, role functioning, social functioning, emotional functioning, pain, fatigue, sleep, appetite, nausea, bowel problems). It was endorsed by the EORTC QOL Group Executive Committee in 2014. This means that the QLQ-C30 can now be administered to obtain both QoL endpoints and utility scores. This will not only reduce patient burden, but has the potential to reduce trial costs associated with PROs, including staff time, printing, data entry, scoring and analysis.

While the QLU-C10D is not quite ready for prime time yet, it will be very soon, and can certainly be included in clinical trials in development now. It can also be used retrospectively for health economic modelling of trials that are closed to recruitment (if they used the QLQ-C30). For more details about this study, please contact the QOL Office (qol.office@sydney.edu.au).

Professors King and Viney are also leading the development of utility weights for the FACT-G. Details will be shared in future issues of the CREST newsletter.

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ANZUP Annual Scientific Meeting 2015

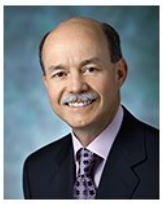
The Australian and New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group is pleased to announce our 2015 Annual Scientific Meeting (ASM) will be held at Sofitel Wentworth Sydney from 12-14 July, 2015.

The ANZUP ASM provides a unique opportunity to bring together the multidisciplinary health professionals involved in researching and treating cancers of the genitourinary system.

Program highlights include:

- State of the art presentations from leading international and Australian experts;
- Up-to-date management and research for prostate and other genitourinary cancers;
- Opportunities for researchers to present their research;
- Clinical trial Concept Development Workshop;
- Community Engagement Forum - A Little Below the Belt;
- Overviews of current and planned ANZUP trials; and
- ANZUP MDT Masterclass.

Outstanding international faculty:

	**Theodore DeWeese MD** Dr. DeWeese is Professor and Chair of the Department of Radiation Oncology and Molecular Radiation Sciences at Johns Hopkins University. He is also Professor of Urology and Oncology at Johns Hopkins and has a broad experience on which to draw regarding basic and translational cancer research.
	**Brian Rini MD, FACP** Professor of Medicine at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University in Cleveland, Ohio. Dr. Rini's primary research has been in renal cell carcinoma (RCC) and prostate cancer, with special focus on antiangiogenic therapy and immunotherapy.
	**Chris Sweeney MBBS** Associate Professor, Department of Medicine, Harvard Medical School and Dana-Farber Cancer Institute. Chris is a clinical oncologist and sits on the Scientific Advisory Committee of ANZUP Cancer Trials Group. His primary research interest is drug discovery and development. His academic focus is management of genitourinary malignancies, with a focus on prostate and testicular cancer.
	**Bertrand Tombal MD, PhD** Professor Bertrand Tombal is Chairman of the Division of Urology and Professor of Urology at the Université Catholique de Louvain (UCL), Cliniques Universitaires Saint-Luc, Brussels, Belgium. He is the current chairman of the Genitourinary group of European Organization for Research and Treatment in Cancer, the leading European academic research organization in the field of cancer.

To register for this event http://www.anzup.org.au/content.aspx?page=asm-registration

Measuring Productivity Effects in Clinical Trials.

The effects of cancer on a patient's health status and quality of life have been and continue to be thoroughly investigated. There are well-developed methods for the inclusion of such effects within an economic evaluation of an existing or proposed health care intervention. However, there is less consensus on how best to assess the impact of a diagnosis of cancer, and the accompanying treatment and long-term morbidity, has on an individual's ability to participate in productive activity (such as work, leisure or other usual activities) for the purposes of its inclusion in an economic evaluation.

Putting aside the question of whether or not productivity effects should be included in an economic evaluation, Tang (2015) provides a comprehensive summary of the main instruments available for use within a trial setting for the assessment of changes in participation in productive activity.1 The strengths and limitations of the available instruments are summarised below.

In discussing these instruments, Tang notes that it is not possible to recommend one measure above any other for a particular project, but that there are specific questions to ask when considering productivity instruments as a means of collecting information for an economic evaluation:

- Is the purpose of the instrument compatible with the intended methods for deriving and estimating productivity costs?;
- Does the instrument capture the relevant data to match the perspective of the economic evaluation?;
- Is a generic or disease-specific instrument relevant for the proposed population?;
- Are there data supporting the psychometric properties of the instrument in a reasonably similar population to that in the evaluation?; and
- What is the practicality of implementing the instrument in terms of its burden on respondents, administrators and potential costs?

Choosing the right instrument therefore needs careful consideration of the goals of the clinical study and the planned economic evaluation. Whether or not an economic evaluation should include productivity changes is likely to depend on the purpose for which it is intended, and how other effects – such as quality of life - are being measured. In the particular project This will be addressed in a forthcoming CREST FactSheet, together with a more in-depth discussion of potential methods for measuring productivity effects.

Productivity Measures – Strengths and Limitations (from Tang (2015)1)

Instrument	Strengths	Limitations
Health and Labour Questionnaire	Comprehensive (absenteeism, presenteeism, unpaid work). Corrects for substitution in unpaid work. Compatible with friction cost valuation.	Feasibility issues – subject to sub-optimal completion rates. Potential cognitive difficulties with direct hour estimating method of assessing presenteeism.
Health and Work Productivity Questionnaire	Extensive development. Validated against meaningful productivity indicators. Multiple versions available depending on objectives and feasibility.	Excludes lost productivity from unpaid work. Applicability of some metrics unclear. Excludes compensation mechanisms, work-team dynamics.
Health-Related Productivity Questionnaire Diary	Includes paid and unpaid work. Feasibility – short questionnaire.	Unpaid work measure doesn't correct for substitution. Includes education as unpaid work. Excludes compensation mechanisms, work-team dynamics. Limited psychometric evidence.

Productivity Measures – Strengths and Limitations (from Tang (2015)1)

Instrument	Strengths	Limitations
Productivity and Disease Questionnaire	Comprehensive (absenteeism, presenteeism, unpaid work, compensation mechanisms, work-team dynamics). Modules for employer's perspectives on productivity costs, administrative and management costs of worker illness.	Excludes lost productivity from unpaid work. Work-team dynamics question requires participation from employer/manager. Limited psychometric evidence on modules.
Quantity and Quality Method	Feasibility – brief. Work quantity and quality concepts intuitive, broad relevance.	Assesses only presenteeism. Uncertainty on amalgamating quantity and quality item scores.
Stanford Presenteeism Scale 13	Multiple perspectives of presenteeism. Able to limit assessment to lost productivity due to a primary health condition. Relatively brief.	Excludes lost productivity from unpaid work. Extent to which respondents can limit productivity lost to one condition is uncertain. Limited psychometric evidence Excludes compensation mechanisms, work-team dynamics.
Valuation of Lost Productivity Questionnaire	Comprehensive (absenteeism, presenteeism, unpaid work, compensation mechanisms, work-team dynamics). Work-team dynamics completed by employees. Allows wage to be related to marginal productivity by deriving adjustment factors for wage multipliers.	Lengthy if all modules completed. Only replaced unpaid work considered. Relies on employees knowing about work-team dynamics to derive wage multipliers.
Work and Health Interview	Reasonable completion time. Validated against administrative data and diary data.	Excludes lost productivity from unpaid work. Excludes compensation mechanisms, work-team dynamics. Limited psychometric evidence.
Work Limitations Questionnaire	Combines empirical observations of productivity with questionnaire productivity metric into on index score. Extensively tested instrument.	Limited to presenteeism. Generalisability of index scoring system unclear since it is derived from one industry.
Work Productivity and Activity Impairment Questionnaire	Includes paid and unpaid work. Extensively tested instrument. Very brief, short completion time.	Activity impairment does not separate unpaid work and leisure activities. Excludes compensation mechanisms, work-team dynamics.
Work Productivity Short Inventory	Includes absenteeism and presenteeism. Able to limit assessment to productivity lost due to different health conditions. Brief (if only a few health conditions are relevant).	Excludes lost productivity from unpaid work. Extent to which respondents can limit productivity lost to different conditions is uncertain (potential for double counting). Excludes compensation mechanisms, work-team dynamics. Limited psychometric evidence.

1. Tang K. Estimating productivity costs in health economic evaluations: a review of instruments and psychometric evidence. Pharmacoeconomics. 2015;33(1):31-48.

ALLG Report: Electronic Data Collection

In a very exciting new development the ALLG is currently rolling out an electronic data collection (eDC) system for its clinical trial program.

In a survey of associate members conducted in April 2013, 83% of respondents saw no advantages in continuing with paper CRF over eDC. This result was not surprising. An electronic system will allow the ALLG Trial Centre staff to control database design and validations checks, rather than relying upon external contractors. It will also streamline processes for data management with savings in resources compared to paper-based methods. Digital systems mean improved data quality as many validation checks are programmed into the database. This means a reduction in data query rates as many queries are resolved in real time.

We anticipate that an eDC approach will contribute to the long-term strategic goals of the ALLG Trial Centre. It will facilitate more timely access to data for analyses specified in the protocol and allow preparation of a library of validated 'reuseable' eCRFs and eDC, thereby reducing trial set up times. With an improved technological base, we will be able to expand collection of patient reported outcomes and health economics in ALLG clinical trials. In the wider perspective, the new system is expected to assist with attraction of further high quality clinical trials and registries, and international collaborations.

Over the last year, various systems have been assessed for useability, cost, licensing and support. The chosen system is XClinical. One important feature of this system is the collection of C-DASH and C-DISC compliant data which constitute consistent data collection fields across the entire clinical trial industry. This feature can better support meta-analysis, and allows for some reuse of the programming required to prepare datasets for statistical analysis.

The rollout of the selected system is already underway in the ALLG Trial Centre. eCRF builds will be chiefly undertaken by Sri Joshi, the Trial Centre data manager, with review of the elements included by the trial statistician, CRA and Chief Investigator/s. The first trial to open on eCRF is expected to be the ALLG CLL07 trial, which will enrol 120 patients over three years. This is an important randomised trial for the benefit of elderly patients with chronic lymphocytic leukaemia.

Any questions regarding the eDC implementation should be directed to Megan Sanders, Program Manager, at Megan.Sanders@allg.org.au.

ALLG Australasian Leukaemia & Lymphoma Group
Celebrating 40 Years of Clinical Trial Research in Blood Cancer 1973 - 2013

Screening Impacts More than Just Health.

The benefits of early screening and detection to improving cancer mortality have long been recognised. However, more recently the universal value of the benefits of screening have been questioned when they are balanced against the broader impact of screening and subsequent interventions on quality of life. In a recent Lancet article, Schroder et al (2014) present long term data from the European Randomised Study for Prostate Cancer (ESRPC).[1] These data show that after 13 years of follow-up the absolute reduction in prostate deaths associated with PSA screening was one per 781 men (95% CI: 490 – 1,929) invited for screening. The longer-term results from the ESRPC confirm those observed in earlier studies of follow-up, that there is a mortality benefit associated with PSA screening of men between the ages of 55 and 69.

However, the screening process itself, and the subsequent follow-up investigations and interventions that might be recommended as the result of any findings might also have effects on morbidity. Heijnsdijk et al (2015) incorporate these morbidity effects into the results of the ESRPC.[2] Using published quality of life data, assessed using a preference scale and expressed as a utility value (on a scale between 0 and 1), they modelled the quality of life effects associated with each stage of the screening process, subsequent interventions, and treatment of prostate cancer. In this manner, their analysis accounted for the overall pathway of

ACORD 2014 and CREST

The Australia and Asia Pacific Clinical Oncology Research Development (ACORD) workshop continues to be a success. The biennial week-long intensive training workshop was held from 14-20 September 2014 at the Magenta Shores resort, NSW, with seventy-two participants and twenty-five Faculty members.

Stephen Goodall from CREST was part of the ACORD faculty at this year's workshop. Stephen contributed in a number of ways including providing lectures on economic evaluation, protocol development sessions, and small group discussions of health economic issues. He also conducted one-on-one sessions, providing advice on protocols and careers.

We are pleased to see a growing interest amongst the next generation of cancer researchers in health economic principles and techniques and the importance of demonstrating cost-effectiveness within clinical trials. Stephen provided advice to approximately 12 protocols, ranging from trial based economic evaluations, cost of care models, evaluations of screening programs and the use of discrete choice experiments to elicit patient preferences for cancer services.

Stephen was also part of the winning quiz team (although this was more association than causality)

The aim of ACORD is to strengthen clinical trial design and to promote continuing success in oncology research in Australia and Asia Pacific regions. ACORD also provides a forum to foster trans-national relationships and to facilitate greater research cooperation across the Asia Pacific region.

We would like to thank the organisers of ACORD, especially Professor Martin Stockler, for including CREST in this successful event.

Screening Impacts More than just Health (cont.)

care from the detection of a potential case of prostate cancer (including potential over-diagnosis) to subsequent treatment of actual cases. They found that while there was an increase in the number of life years gained through adopting PSA screening compared with no screening for a cohort of 1,000 men in all age cohorts modelled, the gain in quality adjusted life years relative to costs declined for those above the age of 63 years. Screening was only considered cost-effective for men aged 55-59, undergoing two yearly testing. Beyond that, the negative quality of life effects of over-diagnosis resulted in a reduction in QALYs relative to the costs, making screening not cost-effective. These results show how apparent health benefits of providing care can disappear when the scope of the analysis is broadened to measure more than clinical and mortality outcomes.

1. Schroder FH, Hugosson J, Roobol MJ, Tammela TL, Zappa M, Nelen V, et al. Screening and prostate cancer mortality: results of the European Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow-up. Lancet. 2014;384(9959):2027-35.
2. Heijnsdijk EA, de Carvalho TM, Auvinen A, Zappa M, Nelen V, Kwiatkowski M, et al. Cost-effectiveness of prostate cancer screening: a simulation study based on ERSPC data. J Natl Cancer Inst. 2015;107 (1):366.

2015 ANZBCTG Annual Scientific Meeting

The 37th Annual Scientific Meeting (ASM) of the Australia and New Zealand Breast Cancer Trials Group (ANZBCTG) will be held in Perth, Western Australia, from 22-24 July 2015 at the Pan Pacific Perth.

The ANZBCTG is the largest independent, oncology clinical trials research group in Australia and New Zealand. For more than 35 years, the ANZBCTG has conducted clinical trials research for the treatment, prevention and cure of breast cancer.

The research program involves multicentre national and international clinical trials and brings together over 700 researchers in 87 institutions throughout Australia and New Zealand. The ANZBCTG has contributed to more than 900 peer reviewed publications and more than 14,000 women have participated in ANZBCTG clinical trials.

The 2015 ASM will host a number of internationally renowned guest speakers and eminent ANZBCTG researchers. International speakers include: Professor Jack Cuzick, Professor Karen Gelmon, Associate Professor Amit Goyal, Professor Linda Vahdat and Professor John Yarnold. Delegates include leading Australian and New Zealand medical practitioners and clinicians, and clinical trials management personnel.

The full and extensive program will include two days of scientific sessions covering timely reviews of breast cancer clinical trials, discussion of new protocols, future clinical trials research and other research developments.

For more information about the ASM, or to register, visit www.anzbctg2015.org. To contact the ASM secretariat, email asm@anzbctg.org or phone 02 4925 5255.

Australia & New Zealand Breast Cancer Trials Group

CREST Workshops: It's Going to be a Busy Year!!!

2015 is shaping up to be a busy year for workshops involving CREST. On March 20th, CREST, with the support of the Western Australian Clinical Oncology Group, is presenting the first of its workshops for the year in Perth; *Understanding Health Economics in Cancer Research.* Demand for attendance at this workshop has been overwhelming, with plans for a second workshop to be held in Perth later in the year.

The second workshop for the year is for consumer representatives of the CTGs, *Health Economics in Cancer Research – A Consumers' Guide*. Slated for 13th April 2015, this workshop is being hosted by the ALLG in Melbourne. Places are still available, so please contact Richard at CREST for details.

Plans are currently underway for three other workshops: a QOL Office/CREST joint workshop in August on the use of quality of life and preference data in cancer research; a CREST workshop on developing and using economic models in cancer trials; and a preference valuation workshop towards the end of the year. Details about these workshops will be provided in the coming months. Remember that CREST is always ready to tailor presentations or workshop sessions to suit your particular trial area or consumer group.

TROG Cancer Research Report – March 2015

Since 1989, TROG Cancer Research has been making a difference to the way cancer is treated and to the outcomes of people and their families affected by the disease. 2015 promises to be another important year for TROG, our research portfolio, Quality Assurance Program and the conduct of clinical trials.

We currently have seven clinical trials in development, 14 active trials and 23 in follow-up. This is a very exciting time as the TROG Central Operations Office branches into the trial coordination of five new studies in 2015.

In 2015, TROG is excited to announce the launch of a new Good Clinical Practice online learning module, which will be a valuable learning resource for our members.

As we celebrate TROG's 26th anniversary in 2015, we reflect on our past achievements and we look to a positive future with a renewed focus on our fundamental goals of collaboration with our stakeholders, organisations and community groups who share our aim of defeating cancer; continuing our quality research on a global scale; and providing the utmost care and consideration for patients, families and our TROG community.

Our community of members now exceeds 1000 and we thank each of them for their support and engagement - TROG's research program is truly a team effort.

TROG's 27th Annual Scientific Meeting will be held from March 24 -26 in Newcastle, NSW. The theme for this year is the 'ongoing evolution of collaborative trials' and our international guest speakers include renowned Radiation Oncologists, Professor Charles Catton from Princess Margaret Hospital in Toronto, Canada; Professor Kevin Franks from St James' Institute of Oncology in Leeds, UK; and Associate Professor Paul Nguyen from Harvard Medical School, USA.

Find out more at www.trog.com.au

What Has CREST Been up to?

Trial Group Collaborations:

- Participation as investigators on nine project grants for the current NHMRC/Cancer Australia grant round.
- Attendance and participation at the PC4 Peer Review Workshop in Melbourne (20th January 2015).
- Attendance and participation at the ANZCHOG Study Concept Worksop in Melbourne (24th February 2015).
- Ongoing advice on the development of trial protocols and data collection forms.

Other Activities:

- Ongoing meetings with the Clinical Trial Group Executive Officers.
- Development of workshops to be held in March and April 2015.