How much risk associated with a biomarker can be accounted for by other prognostic variables in time-to-event outcomes?

Presented by Ms Diana Zannino

When: Friday 4th February, 2011
3.30- 4.30pm

Where: Medical Foundation Building Auditorium
92-94 Parramatta Road, Camperdown
Map ref:
1. campus map
http://db.auth.usyd.edu.au/directories/map/building.stm?location=01B
2. local street map
http://www.whereis.com/index.htm?ref=homeMap#session=MjE=

Abstract: With the proliferation of biomarkers identified in medical research, the importance of individual (or a class of) biomarkers over other prognostic factors is of major interest. In a proportional hazards (PH) regression model, the joint association between variables in the model and the dichotomous event of interest, can be summarised in terms of global performance by the c-index (Harrell-Lee). This index is analogous to the area under the Receiver Operating Curve but allows for censored data. This idea is used to estimate the proportion of a biomarker effect which is accounted for by a set of other prognostic variables by examining changes in the c-index under different PH models. The identification of key prognostic variables may be determined through an exhaustive search subset regression. Provided the different models produced by the exhaustive search are nested, changes in the c-index associated with the successive addition of each variable can be obtained. The percentage change from the c-index, containing just the biomarker of interest is calculated. This approach was applied to a large RCT in diabetes to determine the proportion of eGFR (renal function) prognostic information which is explained by other key variables (HDL cholesterol, HbA1c, etc) on cardiovascular risk.

Bio: Diana Zannino, MSc (Research), is a statistician for the Australasian Gastro-Intestinal Trials Group (AGITG) and Australia and New Zealand Breast Cancer Trials Group (ANZ BCTG). She also works on clinical trials in cardiovascular medicine and assists teaching in the Biostatistics Collaboration of Australia (BCA) program and MPH in the School of Public Health at the University of Sydney.
A model incorporating historical controls into meta-analysis estimates. Illustration of the Begg and Pilote method using data from 2\textsuperscript{nd} line advanced colorectal cancer.

Presented by Mr Chris Brown

When: Friday 10\textsuperscript{th} June, 2011
3.30- 4.30pm

Where: Medical Foundation Building
Level 5, 92-94 Parramatta Road, Camperdown
Map ref:
1. campus map
http://db.auth.usyd.edu.au/directories/map/building.stm?location=01B
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http://www.whereis.com/index.htm?ref=homeMap#session=MjE=

Abstract: There is a proliferation of single-arm studies conducted during development of new treatments and therapies. Is there a sound way to include their estimates of treatment outcomes into subsequent comparisons of treatments? In 1991 Colin Begg and Louise Pilote published a model to incorporate historical controls into a meta-analysis estimate. This method is described and illustrated using data from a recently conducted meta-analysis of 2\textsuperscript{nd} line advanced colorectal cancer. Basic principles of binary outcome analysis are reviewed and we illustrate that the odds ratio (and associated confidence interval) is computable directly from estimates of two proportions and their standard errors. Using this, outcomes from the model incorporating historical controls is compared with that from the small meta-analysis of randomised studies. A summary of the problems and benefits incorporating such data into routine meta-analysis will form the basis for discussion.

Bio: Chris Brown, BSc, has been a Statistician and Research Fellow at the NHMRC Clinical trials centre since 2005. He works closely with Cooperative Trials Group for Neuro-Oncology (COGNO) and is member of the Operation Executive and Scientific Advisory Committees of both this group and The Australasian Lung cancer Trials Group (ALTG) and the Australasian Gastro-Intestinal Trials Group (AGITG). He is currently working on implementing a large Genome Wide Association Study (GWAS) for one the centres cardiovascular trials and also assists teaching in the MPH for the School of Public Health at the University of Sydney.
Detecting Subclusters in Outliers

Presented by Associate Professor Dongseok Choi

When: Monday 11th July, 2011
3.30- 4.30pm

Where: Medical Foundation Building
Level 5, 92-94 Parramatta Road, Camperdown
Map ref:
1. campus map
http://db.auth.usyd.edu.au/directories/map/building.stm?location=01B
2. local street map
http://www.whereis.com/index.htm?ref=homeMap#session=MjE=

Abstract: Detecting Subclusters in Outliers

Medical research is often interested in finding subgroups in an outlier group. For example, a certain medical condition can be more frequent in a small group that is different from the majority of population. One approach to find groups in a data set is using cluster analysis. Cluster analysis has been widely used tool in exploring potential group structure in complex data and has received greater attention in recent years due to data mining and high dimensional data such as microarrays. In this presentation, I will introduce split-and-recombine procedure and its application for a medical data set. In addition, analysis results of the same data using other clustering methods will be discussed.

Bio: Dongseok Choi is Associate Professor of Biostatistics at Oregon Health and Science University, Portland, Oregon, U. S. A. He got his PhD in Statistics from the University of Chicago in 1999. His research interests are mixed-effects quantile regression, clustering methods for microarrays/proteomics, predicting motif binding sites, spatial-temporal models and geographic information system (GIS), and statistical methods for surveys. Before joining the OHSU, he worked at Organisation for Economic Cooperation and Development, University of California Santa Barbara and Portland State University.

He has been actively serving for international statistical professional societies. He is the former President of the Oregon Chapter of American Statistical Association (ASA). He served as the Poster Chair for the Program Committee of 2007 Joint Statistical Meeting, for the International Relations in Statistics Committee of the ASA from 2005 to 2010, and currently for the Program Committee of the International Chinese Statistical Association. In addition, he has been a member of Statistics Without Borders since its inception. He is currently the President of Korean International Statistical Society.
Impact of censoring on time-to-event problems in the presence of competing risks

Presented by Mr Mark Donoghoe

When: Friday 5th August 2011

3.30- 4.30pm

Where: Medical Foundation Building
Level 5, 92-94 Parramatta Road, Camperdown
Map ref:
1. campus map
http://db.auth.usyd.edu.au/directories/map/building.stm?location=01B
2. local street map
http://www.whereis.com/index.htm?ref=homeMap#session=MjE=

Abstract: Competing risks are often present in time-to-event data in clinical trials – for example, non-cancer death preventing the observation of local recurrence – and methods to account for these are becoming more common in mainstream statistical analyses. Common approaches include those based on log-rank type tests (Gray) or cumulative incidence regression (Fine and Gray), which use the distribution of censored observations to weight observations of competing risk events. However the impact of events/censoring in these approaches is still unclear. Through extensive simulations, we examined two aspects of this problem: the amount of competing risk present in a proportional hazards model, and the pattern of censoring between groups in the presence of competing risks. The different approaches were also examined on actual data for time to relapse in patients treated for multiple myeloma.

Bio: Mark Donoghoe, BSc (Hons), has worked as a statistician at the NHMRC Clinical Trials Centre since 2007. He has been involved in analysis of the large-scale FIELD study in cardiovascular event prevention, as well as trials for the Australia New Zealand Gynaecological Oncology Group (ANZGOG) and the Australasian Gastro-Intestinal Trials Group (AGITG).

Dr Belinda Kiely

When: Wednesday 21st September, 2011
11:30am – 12:30pm

Where: Medical Foundation Building Auditorium
92-94 Parramatta Road, Camperdown

Map ref:

Biography
Belinda Kiely is a medical oncologist in the third year of her PhD studies at the NHMRC Clinical Trials Centre. Her PhD is titled ‘Estimating survival duration and communication of prognostic uncertainty in patients with advanced cancer.’ Belinda was one of 54 promising cancer researchers presented a Conquer Cancer Foundation Young Investigator Award at the 2011 American Society of Clinical Oncology Annual Meeting in Chicago, Illinois. Her award is to support a 12 month project titled “Evaluating an iTool to estimate and explain survival time scenarios to people with advanced cancer.”

Abstract
Most patients with advanced cancer want information about their expected survival time and many want specific estimates of the best case, worst case and typical scenarios for survival. We have developed a web-based tool (iTool) to assist oncologists estimate and explain individualized scenarios for survival to patients with incurable cancer. The aim of this study is to evaluate: the attitudes of oncologists to using the iTool to explain survival times during clinical consultations; the attitudes of advanced cancer patients and their family members to receiving survival information formatted as three scenarios (best case, worst case and typical) and the attitudes of other health practitioners involved in the patient’s care to receiving a printed summary of the survival information. If found to be helpful, the iTool has potential to significantly improve communication of prognosis to people with advanced cancer.
The MAUCa Project: Multi-Attribute Utility measures for Cancer clinical trials

Professor Madeleine King & Dr Dan Costa

When: Friday 7th October, 2011
3:30pm – 4:30pm

Where: Level 5 Training Room, Medical Foundation Building
92-94 Parramatta Road, Camperdown

Biography
Professor Madeleine King is the Cancer Australia Chair in Cancer Quality of Life. She is health researcher whose experience ranges across biostatistics, psychometrics and health economics. Her main research interest is the measurement, analysis and interpretation of health-related quality of life and other patient reported-outcomes. Madeleine is a former President of the International Society for Quality of Life Research.

Dr Dan Costa is the MAUCa Project Officer. He has a PhD in Experimental Psychology and a developing portfolio of post-doctoral collaborations as a psychometrician.

Abstract
The MAUCa Consortium was formed in 2010 with the overarching aim of facilitating the inclusion of HRQL information in health policy decisions about funding new treatments for cancer by developing two cancer-specific multi-attribute utility instruments (MAUI) from the two most widely used cancer-specific health-related quality of life measures, the QLQ-C30 and the FACT-G. Hence ‘MAUCa’: Multi-Attribute Utility in Cancer. The Consortium has an international multidisciplinary membership of 18 health economists, oncologists, psychologists, behavioural scientists, psychometricians and biostatisticians from Australia, UK, Europe, Canada and USA.

In this presentation, Prof Madeleine King (founding Chair of the MAUCa Consortium) and Dr Daniel Costa (MAUCa Project Officer) will outline the aims, methods and preliminary results of Stage 1 of the QLQ component of MAUCa, which is funded by an NHMRC Project Grant 2010-2012.
NHMRC CLINICAL TRIALS CENTRE
RESEARCH SEMINAR

“How the data you collect & analyse in clinical trials is used in the real world”

Hannah Verry & Toby Gould

When: Thursday 3rd November, 2011
3:30pm – 4:30pm

Where: Level 5 Training Room, Medical Foundation Building
92-94 Parramatta Road, Camperdown

Map ref:
1. campus map http://db.auth.usyd.edu.au/directories/map/building.stm?location=01B
2. local street map http://www.whereis.com/index.htm?ref=homeMap#session=MjE=

Biography
Hannah Verry has a Bachelor of Economics from the University of Queensland and is currently enrolled in a PhD through the Sydney Medical School entitled “Accounting for the economic burden of mortality in Australia and opportunities for intervention”. Hannah has worked at the NHMRC Clinical Trials Centre since 2009 and is involved in performing health economic evaluations using data from clinical trials. She has expertise in modelling the cost effectiveness of cancer interventions.

Toby Gould joined NHMRC Clinical Trials Centre in July after working for the Victorian Department of Health where he was responsible for guiding Victorian government investments into translational cancer research. Prior to his role in government Toby worked in the biotechnology sector specialising in the development of In-Vitro Diagnostic tests for Human Papilloma Virus screening and cancer mutation detection applications.

Toby’s work at the NHMRC Clinical Trials Centre is focussed on the appraisal of funding applications for new health care technologies that are being considered for listing on the Medicare Benefits Schedule. These assessments are undertaken on behalf of the Federal governments Department of Health and Ageing. Toby’s main interest is in the development and implementation of techniques for the economic evaluation of biomarker tests.

Abstract
New health care interventions can no longer afford to rely on demonstrating effectiveness alone in order to change clinical practice. Decision makers around the world are increasingly concerned with cost-effectiveness, which can be seen as a measure of ‘bang for your buck’ when spending precious health budget dollars. In this seminar, Hannah will present a decision model of sentinel node biopsy for patients with early stage breast cancer. The model synthesises health outcomes, costs and patient preferences from a number of RCTs in order to estimate the long term effectiveness and cost-effectiveness of the procedure.

Following this, Toby will take a broader perspective and outline how clinical trial data and results are considered as part of the decision making process of whether a new health care intervention should receive government subsidy. This part of the seminar aims to explore how both clinical and economic considerations are balanced during the health care funding decision making process, as well as highlight the value of collecting data for use in economic models during clinical trials.