84 INVITED

Response assessment in new drug trials

A. Peet[1]. [1]*University of Birmingham, Cancer Sciences, Birmingham, United Kingdom*

The conventional method for assessing response in solid tumours is serial measurement on anatomical imaging, usually CT or MRI. This approach has disadvantages: the size of the tumour is likely to decrease later than the response at a cellular level and assessment does not take account of the fact that the whole mass may not be viable tumour. New imaging techniques, commonly grouped under the term functional imaging, are increasingly addressing these problems by probing tissue properties rather than anatomical structure.
There are two main technological approaches to functional imaging, one based on extensions of magnetic resonance imaging and the other based on advances in nuclear medicine.
Advanced magnetic resonance imaging methods have the advantage that they can be readily coupled to conventional MR imaging investigations with little additional equipment required. There are several complimentary techniques and they are commonly being used together in a multimodality approach. Magnetic resonance spectroscopy provides a quantitative profile of metabolites and lipids. Clinical studies have already identified markers of tumour response, in particular total choline. Animal studies have shown polyunsaturated fatty acids to be a very early marker of apoptosis. Diffusion weighted imaging provides a useful marker of cellularity and correlates with cell death. Studies have shown diffusion weighted imaging can be an early maker of tumour response. Perfusion may be studied by a number of techniques, the most common being dynamic contrast enhanced MRI. These techniques have become of particular relevance with the interest in anti-vascular and anti-angiogenic treatments. Perfusion imaging gives a direct measure of drug action and studies have shown alterations when these agents are effective. Dynamic nuclear polarization is an emerging method for producing molecular tracers of metabolism which can be detected by magnetic resonance spectroscopy. Pyruvate is a promising tracer for tumour response and is entering clinical trials. Molecular imaging may be undertaken by the addition of gadolinium atoms to molecules designed to attach to specific targets allows them to be visualized on conventional MRI. Molecular imaging is of particular relevance to novel targeted agents and is likely to become of increasing interest in the future. Nuclear medicine techniques are well established and the advent of single photon emission computerized tomography (SPECT) and positron emission tomography (PET) has allowed multi-slice images to be produced. Combining these techniques with CT and MRI allows the functional images to be registered accurately with high quality anatomical imaging revolutionizing their use in cancer. 19F-deoxyglucose PET has become well established as a marker of active tumour. However, more specific markers are becoming available and the exquisite sensitivity of PET currently makes this the targeted molecular imaging modality of choice. PET tracers can also be made from drugs making in vivo pharmacokinetics available. Combining MRI and PET in a single scanner allows high quality structural and multimodality functional imaging and promises to revolutionize response assessment of new drugs.

86 INVITED

Ethical aspects of early phase clinical trials in children

F. Doz[1]. [1]*Brain Tumour Committee, Paediatric onoclogy, Paris, France*

The objective of a phase I trial in paediatrics is to determine the recommended dose of a new treatment in children while evaluating its toxicity. These trials are proposed when no effective curative treatment is available. The probability of a benefit in terms of disease control is certainly very low, but greater than zero.
We will present the work conducted by a collaborative group of parents, healthcare personnel and a philosopher which concludes that phase I therapeutic trials can be considered to be an ethically acceptable proposal provided the criteria and risks of inclusion in such a trial are clearly defined. We will discuss the main elements of this inclusion process and try to provide guidelines for healthcare personnel and parents. Furthermore, we will present specific preliminary information from a current prospective study about information and consent process for early phase clinical trials. The need for information provided gently but honestly, the importance of a sufficient time to think about the proposed trial, a two-sided dialogue and partnership between the various actors, and the priority given to the child's best interests, constitute the decisive elements to guide the proposed inclusion in an early phase trial. These conditions help to ensure that a decision is reached which appears to be morally founded for all parties, while allowing the child to remain alive up until the end, i.e. a human being capable of relating. This decision allows parents and healthcare personnel to retain a good self-image; if the child dies, it is by keeping their self-esteem that parents can live with their bereavement and healthcare personnel can reinvest in other patients.

Advocacy Session (Mon, 21 Sep, 16:15−17:45)
Access to clinical trials

87 INVITED

Clinical trials registries and databases

D. Ghersi[1]. [1]*World Health Organization International Clinical Trials Registry Platform, Geneva, Switzerland*

In 2005 a World Health Assembly resolution called for the establishment of "a platform linking a network of international clinical trial registers to ensure a single point of access and the unambiguous identification of trials". This resulted in the establishment of WHO's International Clinical Trials Registry Platform (ICTRP), the core principle of which is that the registration of clinical trials in a publicly accessible registry is a scientific, ethical and moral responsibility. In 2007 the ICTRP published its online Clinical Trials Search Portal which allows users to search the data sets provided by registries that meet WHO's standards for quality control and content. Registries that currently meet these criteria are based in Australia, China, Germany, India, Iran, the Netherlands, Sri Lanka, the UK and USA. On 3rd July 2009 the portal contained records relating to 86978 trials, of which 15742 were identifiable as being trials in cancer. A more detailed search reveals that there has been a significant increase in the number of registered trials recruiting participants with cancer over a 5 year period with 703 being registered in 2004 compared with 2780 registered in 2008. Although the need to register trials in a publicly accessible database has become accepted by many there are still barriers to achieving full compliance, particularly in developing countries. We need to consider how we may better use the information these registries contain, how we might make the data they contain more accessible, and the opportunities they give us to build better systems for clinical trials oversight.

90 INVITED

The patient perspective

R. Wilson[1]. [1]*Sarcoma UK, Ludlow, United Kingdom*

The patient advocacy view of clinical trials goes beyond the crucially important aspects of information about trials and access to them which are commonly presented as primary patient interests. The presenter has been treated on a trial, helped and advised other patients considering or entering trials, taken part in the development and review of new studies, is involved in funding review, and has used trial evidence to support advocacy cases in regulatory review. He has also worked with strategic management and has developed a deep understanding of how the evidence from trials informs (or sometimes fails to inform) treatment and service development, through guidelines and health technology appraisals. He draws on his own wide-ranging experience to present a fresh and challenging view of clinical research and what can be developed to help clinical trials deliver greater benefit to patients.

Tuesday, 22 September 2009

Scientific Symposium (Tue, 22 Sep, 09:00−11:00)
Researching complex clinical issues in cancer care

91 INVITED

Nursing-sensitive outcomes: what are they and should we be measuring them?

D. Doran[1]. [1]*Lawrence Bloomberg Faculty of Nursing -, Nursing, Toronto, Canada*

Background: Nurses, like all health professionals, are being asked to assume greater accountability for the improvement of health care system costs and outcomes. Accountability means answering for one's actions and the consequences of those actions. Accountability is one of the hallmarks of the professions. Patient outcome is a measure of the consequences of health care actions. Nursing sensitive patient outcomes are those that are

relevant based on nurses' scope and domains of practice and for which there is evidence linking nursing interventions to outcome achievement.
Purpose: This paper provides an historical view of nursing sensitive outcomes measurement and presents the findings of two empirical studies exploring outcome indicators sensitive to nursing care.
Methodology: A scoping review of the theoretical and empirical literature was conducted. Evidence for the following nurse-sensitive outcomes was reviewed: functional status, symptoms, mortality, health care utilization, safety, and satisfaction. Two studies, one involving acute care, and the second involving acute care, home care, and long-term care settings, were conducted testing the outcomes for sensitivity to nursing care and evaluating approaches to measurement. The first study involved secondary analysis of hospital discharge abstract databases, focusing on the relationship between nurse staffing, nurse education, and 30-day hospital mortality. The first study employed a longitudinal descriptive design; data were collected at the time patients were admitted to health services, daily for symptom outcomes, and at health care discharge. Data on nursing interventions were collected through chart audit.
Results: High quality care is conceptualized as having three dimensions: ensuring that care is safe, effective, and provides patients with the most positive experience possible. The outcome domains and approaches to measurement were found sensitive to nursing interventions and nurse staffing variables in acute care, home care, and long-term care settings.
Conclusion: Nursing sensitive outcomes measurement is feasible and there are valid and reliable measures for assessing nursing sensitive outcomes. Patient-centred care underscores the importance of a multi-disciplinary approach to outcomes measurement and should include the patient's perspective in outcomes measurement. This paper concludes with a discussion of where nursing sensitive outcomes measurement fits within a patient-centred approach to care.

92 INVITED

Selecting appropriate outcome measures for exercise interventions in cancer survivors

K.S. Courneya[1]. [1]*Univeristy of Alberta, Physical Education, Edmonton, Canada*

Background: Selecting appropriate outcome measures for clinical exercise trials is a balance between the desire to show positive results (what is likely to change) and the desire to demonstrate clinically meaningful results (what is important to change). Moreover, selecting an appropriate primary outcome measure will depend on the patient population, the type of exercise intervention, and the timing of the exercise intervention (e.g., during treatment, survivorship, end of life). The purpose of this presentation is to provide an overview of: (a) the various outcome measures that have been examined in previous exercise trials in cancer survivors, (b) theoretical models that may be useful in organizing, selecting, and analyzing outcome measures for exercise trials, and (c) exercise trials that have tested some of the proposed theoretical relationships among the various outcome measures.
Materials and Methods: An overview of the literature of previous exercise interventions trials in cancer survivors and theoretical models of exercise outcomes in cancer survivors.
Results: Exercise interventions in cancer survivors have typically measured multiple outcomes from multiple health categories including health-related fitness (e.g., aerobic capacity, muscular strength and endurance, flexibility, body composition), objective physical functioning (e.g., chair rise, stair climb, lifting/reaching), patient-reported physical functioning (e.g., physical functioning subscales from various quality of life scales, late-life function scale), activities of daily living (e.g., housework, gardening, shopping), biomarkers (e.g., insulin, immune function), psychosocial functioning (e.g., depression, anxiety, stress, self-esteem, happiness), and quality of life (e.g., various quality of life scales). Few studies have included treatment or disease outcomes. Moreover, few studies have included outcome measures from all the key health categories or followed a theoretical model in the selection of the outcome measures. Finally, few studies have examined whether changes in health-related fitness or objective physical functioning mediate changes in patient-reported outcomes or treatment/disease outcomes.
Conclusions: Exercise researchers have included a wide variety of outcome measures in their trials with the most common being health-related fitness, psychosocial functioning, and quality of life. Moreover, many exercise researchers have selected a health-related fitness outcome as their primary outcome. Although such an outcome has a high likelihood of changing, it may not be considered clinically meaningful by itself. Consequently, researchers should consider including additional clinically relevant outcomes for cancer survivors and examine the link between fitness and functioning, and the clinical outcomes. Moreover, selecting a health-related fitness outcome as the primary outcome typically requires a much smaller sample size to demonstrate efficacy which usually leaves the trial underpowered for other clinically important outcomes. Ideally, the selection of outcomes measures should be influenced by the needs of the particular patient population and follow a theoretical model, most likely including measures of health-related fitness, objective physical functioning, patient-reported physical functioning, activities of daily living, psychosocial functioning, quality of life, and treatment/disease outcomes.

93 INVITED

Design and methodological challenges in cancer-related quality of life research

T. Kroll[1]. [1]*University of Dundee – School of Nursing and Midwifery, Alliance for Self Care Research, Dundee, United Kingdom*

The presentation will examine challenges related to the design and methodology of research that focuses on capturing 'quality of life' in people with cancer. The relationship between health-related and general quality of life (QoL) concepts and the underlying assumptions (e.g. stability, dimensionality, scope) will be reviewed and critiqued. Specifically, issues such as multi-morbidity, complex marginalisation, transition periods (childhood, adolescence, adulthood, old age; stages of cancer) will be explored with regard to quality of life concerns. Questions about who contributes to the conceptualisation of (health-related) QoL and whether QoL can ever be considered an outcome measure (as opposed to temporary process measure) will be discussed. The conceptual debate will then be followed by a brief examination of how quality of life is currently 'assessed' in various clinical and non-clinical settings and contexts.
Several quality of life measures are used in the literature (e.g. Life Satisfaction Index, Visual Analog QoL scale, Quality of Life Index, Quality of Life Index, Philadelphia Geriatric Morale, Quality of Life Scale, Faces Scale and Hospice Quality of Life Index. They vary in the number of items, content domains, degree of internal and external validity and cancer specificity. Findings from a review of systematic reviews in the area of cancer-related QoL studies show that primary studies frequently combine multiple QoL measures with psychometric properties that have been ascertained to a varying degree. Rarely, measures are adapted and examined for their sensitivity and specificity in distinct environments and with subgroups of cancer patients.
Frequently, narrow inclusion/exclusion criteria create an artificially constrained sample whose QoL is assessed (usually but not always the same narrow set of individuals that matched the validation criteria for the instrument) and then extrapolated to a larger group. Study instrumentation itself may rule out study participation of people with communication, mobility or sensory impairments. If sampling, consenting and study administration procedures are not adjusted. Non availability of alternative formats to obtain consent, exclusive reliance on proxy respondents, insufficient researcher training, reliance on a single QoL measure may compound inaccuracy of findings. Few research publications indicate whether specific accommodations were made for people with cancer-related impairments to participate in a research project. Non-inclusion in QoL studies may have serious consequences There is no guarantee that health interventions are effective in the same way or may even carry risks for individuals whose 'QoL' has not been considered in primary studies. Examples from effectiveness and observational QoL studies will be used to examine specific problems.
The presentation will conclude with a number of key recommendations for future cancer-related QoL research.

94 INVITED

Patient-reported outcomes in cancer research

G. Velikova[1]. [1]*Cancer Research UK Centre, University of Leeds, Leeds, United Kingdom*

As a result of new and improved therapeutic interventions, cancer survival rates are improving and the nature of cancer care is changing. Many cancers are now being managed as chronic diseases, treated over a prolonged period of time to achieve disease control, prolongation of life and palliation. High quality cancer care aims to improve a range of patient outcomes including not only survival but also important subjective outcomes such as symptom control, functioning and health related quality of life. Meeting those challenges requires routine use of robust and valid measures of patient self-reported outcomes in cancer research and care.
This presentation will describe the current state of the art in this research area in 3 sections:

1. Development and evolution of patient-reported outcome measures (PROMs), including health status questionnaires, quality of life instruments, screening measures for psychological morbidity and measures focusing on single concepts such as pain, fatigue, satisfaction with care.
2. Using PROMs in clinical trials as primary or secondary outcomes of treatment. Examples will be given from trials successfully implementing PROMs. The impact on those findings on clinical decision-making will