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The NHMRC Clinical Trials Centre at the University of Sydney runs large multicentre investigator-initiated clinical trials, takes part in trials of national and international collaborative trial groups and contributes expertise to trials run by others. It also:

- undertakes research into trial methods and is recognised through publications as a leader in trial methodology
- reviews and synthesises evidence from completed trials, and is at the forefront of developments in methods, such as prospective meta-analysis
- advises on trial design and operation, and randomises patients and analyses data for other groups conducting trials, particularly through its Outreach program
- takes a lead in proposing new directions for trial research in Australia, particularly with regard to integrating clinical trials with national policy and clinical practice
- offers placements for postgraduate students in all of these areas
- runs short courses in the design and conduct of clinical trials as part of its undertaking to train people for Australian medical research.

Core funding is provided by the NHMRC, and specific projects are funded by government, public and private institutions and the pharmaceutical industry.

The CTC is at two sites in Camperdown in inner Sydney — the Medical Foundation Building on Parramatta Road and on Mallett Street.

This report covers the CTC’s achievements for the biennium 2008–2009.
20-years on

In 2009 we celebrated our 20 years of research and evidence with a one-day symposium. Leaders from academic and research institutions and government underscored the fundamental role of trials research in clinical practice, policy and health, and explored the likely way ahead. Australia faces rapid aging of the population coupled with increases in the cost and sophistication of both health care and medical research. In addition, biological and genetic clinical research, which can lead to personalised care for patients, will raise new challenges.

The CTC and its collaborators are in a strong position to contribute to Australia’s health research over the coming years. From a handful of staff in 1988, the CTC has grown to about 150 in 2009. Government grant funding for the two years, 2008–2009, was over $24 million, supplemented by substantial funding won from industry for clinical trials. Dedicated research staff and increasing funds have led to success in publication: in 2008–2009, we contributed to over 90 published research articles, most in high-impact journals, and 9 reports for government. CTC staff gave over 80 research presentations at national and international conferences.

We have been at the forefront of research on new treatments and establishing the optimal use of existing treatments.

Central to the success of these activities have been the extensive networks of collaborators we work with and our strong and enduring partnerships with government, nongovernment organisations and industry. We actively work with 7 collaborative groups in oncology on current trials and participate in other projects more broadly. Our research covers cancer types representing about 75% of the cancer disease burden in Australia. A grant from Cancer Australia, together with other grants, has helped us to establish new collaborative groups and to appoint a new chair in health economics, Professor Deborah Schofield.

In collaboration with associated groups we currently have over 50 trials open to recruitment, in follow-up or about to commence. Completed trials have resulted in many exciting discoveries. In FIELD, the finding that fenofibrate can reduce the risk of amputation and damage from small-vessel disease opens up a new treatment option for patients. The SNAC trial showed that sentinel-

CTC Executive: Wendy Hague (clinical trials program director), Kim Russell-Cooper (general manager), Anthony Keech (deputy director) and John Simes (director).
node-biopsy-based management of early breast cancer leads to better quality of life and less arm morbidity than more extensive surgery of the axilla. In advanced colorectal cancer, the K-ras gene type can now identify patients who will benefit from cetuximab, a molecular targeted therapy (Co.17 trial). In LIPID, novel biomarkers linked to coronary risk have been identified, and a study differentiating measurement error and true change in cholesterol monitoring revealed that much routine testing could be too frequent.

One of our research strengths is to devise new methods and apply them to trial datasets to strengthen and augment trial findings. A major international prospective meta-analysis of the Cholesterol Treatment Trialists’ Collaboration, coordinated by the CTC and the Clinical Trials Service Unit, Oxford, confirmed the benefits of statin therapy in patients with diabetes in an individual-patient-data analysis of a cohort from 14 trials. A neonatal meta-analysis study showed that unrestricted oxygen therapy for premature infants had potential harms without clear benefits. This practice has been abandoned, but more targeted oxygen therapy is being assessed in ongoing trials (BOOST II). Risk models and improved methods for diagnostic test evaluations have allowed better application of new evidence from trial data to individual patients. For example, a study of complex measures of test accuracy combined with available clinical evidence has determined the incremental accuracy of magnetic resonance imaging and its potential contribution to cancer staging.

All of the research we undertake at the CTC—either by generating relevant evidence through appropriate trials or by developing better methods for integrating trial evidence and other information—is based on ensuring that trial evidence will have optimal impact on future practice. These pages report many examples of clinical trials and related research that should lead to improvements in health outcomes from future changes in clinical practice and health policy.
In 2008 the CTC moved from the Mallett Street campus to two sites in Camperdown, the Medical Foundation Building, 92–94 Parramatta Road, and 6–10 Mallett Street.
20 years of the NHMRC Clinical Trials Centre

THE FIRST DECADE

The CTC was founded in October 1988 in response to a national need for relevant evidence to underpin the individual clinical decisions of Australian doctors. The National Health and Medical Research Council funded the centre at the University of Sydney, on the basis of its international reputation as a centre of excellence in medical research, diverse research infrastructure, and large departments of public health and medicine.

Work began with two staff: Dr John Simes, the director, and his assistant. Within a year, the CTC had acquired biostatisticians, computer systems experts, trial coordinators, research fellows and a deputy director. By the end of 1989, two international cardiovascular trials, LIPID and the TPA/SK mortality trial, and several large cancer trials were up and running, with over 2000 patients recruited.

From the start, the centre’s educational role was central to its goals of improving the quality of clinical trials in Australia and being relevant to clinical practice. For the staff, this meant teaching and supervising postgraduate students and turning out short courses in statistics and trial management.

By 1996, trials in germ cell cancer, breast cancer and cardiovascular disease were operational, and several million dollars in annual funding flowed from industry and government. Growing staff numbers prompted the move from the university campus to the Mallett Street campus in December 1996.

Between 1997 and 1998, the CTC began to take on more trials and branched out into trials methodology. It also developed its advising and consulting role.

THE SECOND DECADE

The number and breadth of the trials increased and included important initiatives in neonatal research. Research into trials methodology led to better ways of designing and conducting trials. Data from continuing and completed trials became a rich source for analysis in substudies, secondary studies (such as cost-effectiveness analyses) and meta-analyses. Research activities that added value to trial results became an important focus.

Memorable highlights of this period were the international clinical trial symposiums, in 1999, 2002 and 2007, and the long-awaited Australian New Zealand Clinical Trials Registry, established in 2005.

THE THIRD DECADE

Now, about 150 people work at the CTC. Current trials range from about 50 patients in some of the cancer treatment trials to thousands still being followed up in the international FIELD diabetes trial. The CTC’s first major multicentre trial, LIPID, is still following up nearly 7000 patients of the original 9014, 19 years from its first randomisation.

The CTC remains focused on the future. In part because of clinical trials of past years, Australians are living longer, so their health needs may be changing. For example, cancer survivors want better quality of life. In the CTC’s third decade, the issues will be: how to conduct more trials in Australia in the face of cost barriers; how to make trials research an integral part of health care; going beyond drug trials to assess other types of therapy; finding out how individual patients respond to treatment, in biotechnology and preference studies; and answering important clinical questions in new areas (such as indigenous health). Future progress will rely on collaboration among many research networks as well as groups in universities, government and industry.
20 years of clinical trials: a symposium

New evidence, better treatment, changed practice

In 2008 the Clinical Trials Centre reached a milestone: 20 years of research generating evidence for high-quality health care. At a celebration symposium, leaders from government, industry, research and the community at large reviewed past and recent trial successes and addressed the following questions and issues concerning the next 20 years.

Research is likely to be shaped by the continued aim of improving practice and health outcomes, but with new challenges and constraints—particularly the need for even larger patient numbers to reliably demonstrate treatment benefits, the ever-increasing costs of new trials and developing new treatments; the growing demands of regulatory and ethical requirements; and the challenges and opportunities associated with new technologies, especially molecular targeted therapies and e-health. Trials need careful planning and conduct to ensure that we get the best evidence and that it can be applied effectively where it is needed. Central to this is answering the right clinical questions in the most efficient and effective ways.

**HOW CAN WE MAKE SURE THAT CLINICAL TRIALS ASK THE RIGHT QUESTIONS?**

This is a complex issue and involves clinical investigators with relevant trial expertise working with basic scientists (helping to identify potential new treatments), clinicians (with knowledge of current best standard care) and patients or consumers (to ensure questions relevant to the patients’ perspective are addressed). Prioritising potential trials will also depend on the burden of disease (from national morbidity statistics), knowing which studies are already being done (from trial registers), and reviews of current evidence (defining best care and ensuring questions have not already been answered).

**WHAT WILL AFFECT DATA AND METHODS IN THE NEXT 20 YEARS?**

As clinical research progresses, patients participating in trials are healthier, so trials seek smaller incremental improvements from treatment. This means that larger numbers of participants are needed to show a difference.

Added to this, patients can now be stratified by biological markers into smaller groups to allow more personalised use of therapies according to individual profiles. For example, many new cancer therapies are particularly effective but for only a subgroup of patients, depending on the genetic make-up of the cancer. This means we have the challenge of finding sufficient patients for each new trial as well as less return on cost from the developed therapies (due to the smaller future market).

Triallists are already faced with the quandary that patients are very different: there may be more biological markers and genetic factors in the patients than there are types of event to be measured. This has implications for methods and trial operation. First, methods of incorporating prognostic and predictive biomarkers will be important. Second, tissue banking and blood sampling should be a routine part of trials (with appropriate ethical and privacy safeguards), so that samples can be tested in, say, 10 years’ time, after other treatment discoveries. Synthesising that information requires novel methods.

**EFFICIENCY IS A GOAL IN TRIALS RESEARCH**

Appropriate trial design can maximise efficiency. The event or disorder being measured in a trial has to be frequent enough to allow valid statistical analysis. Combining various types of clinical event and looking at the total (a composite outcome) leads to more statistical power and more ability to show an effect. Combining several smaller studies can be an alternative to very large trials. Systematic reviews of evidence and prospective meta-analysis are established but evolving methods for obtaining evidence from combined studies. For this to work, all trials must be registered so that none are excluded. Data can also be combined and reanalysed with data from past trials, a method that is particularly useful when augmented by new knowledge, as in studies of new biomarkers.

Strategies to maintain clinical research will require ways of reducing its considerable expense. Regulatory requirements, ethical requirements, contracts, insurance and so on are great administrative burdens for research. We need to ensure that those demands are no more than in routine clinical practice.

The types of trials that obtain pharmaceutical-industry funding are those with a potential commercial return. The private sector model has the advantage that only treatments that work are likely to be developed, but the drawback is that useful treatments without commercial
value can be neglected. Therefore, trials research that improves health presupposes that some of the funding must come from government.

Making clinical trials a routine part of clinical practice would lead to administrative efficiency and thus lower costs. One of the main costs of research is generating and accessing data. Electronic medical records could allow every patient to contribute to research evidence by linking streamlined pragmatic or even virtual trials into health records.

Governments may fund studies because it would be more cost-effective than paying for services without evidence of their effectiveness and value. For other activities, an idea worth exploring is a global health research fund that could require investment from government and industry to support questions of major public health importance.

**TRIALS IN HARD-TO-RESEARCH AREAS: A CHALLENGE TO CURRENT FUNDING ARRANGEMENTS**

Trials that go beyond drugs — such as physical interventions, systems of care, rehabilitation programs, paediatric trials and surgery — often do not fit a commercial model, so governments need to fund them directly or improve the regulatory framework for industry to do so. One example where this has been done is in the United States, where licences for certain drugs have been extended in return for a commitment to use them in paediatric trials.

**HOW CAN TRIALS BECOME MORE RELEVANT TO CLINICAL PRACTICE?**

Evidence will not be applied if the clinical outcomes do not reflect the full clinical picture: averting clinical events or improving survival may not be enough without quality of life. In addition to this, the trial evidence must be relevant to individuals. Our methods must include exploring the generalisability of results and the individual differences among patients.

Evidence-based management of patients as a criterion of hospital performance would improve the application of evidence to practice generally. One current example is the use of statins, beta-blockers and anticoagulants in protocols of treatment after myocardial infarction.

**WILL CLINICAL TRIALS REMAIN VIABLE IN AUSTRALIA?**

The growing costs for trials research, whether by the pharmaceutical industry or cooperative trial groups, relate to ethics and governance as well as conduct of trials. Australia will have difficulty competing on costs, but by starting small with a grant from government for capacity building or part of a trial, we can build a framework of expertise and knowledge for major international trials. Australia’s advantage is quality. Although local patients may be scarce, we have the opinion leaders, the intellectual resources, and the ability to design and analyse studies and undertake biological substudies. These attest to a capacity to continue to generate new evidence for better treatment and changed practice in the next 20 years.

Below: 20-year symposium panelists, Warwick Anderson, chief executive officer of the NHMRC; Sally Crossing (centre), representing health care consumers; and Kevin Lynch, Celgene Australia.
## Funding

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<td>Pharmaceutical industry*</td>
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<td>Other</td>
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<td><strong>16,156,760</strong></td>
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* Includes Amgen, Abbott Laboratories, Arcagly-Gineco, Aventis Pharma, Bristol-Myers Squibb, Fournier Pharma, Merck Serono, Merck Sharp & Dohme, Norvatis, Pfizer, Roche, Sanofi, Schering Plough, Solvay

Pictured (left to right): Mark Chatfield, Angus McDonald and Sandra Healey, and Nina Stromqvist
Our capacity to conduct high-quality clinical trials has grown through expansion in our infrastructure and consequent strengthening and streamlining of processes for conducting trials. Consolidation of resources of multiple collaborative clinical groups through the CTC leads to economies and ensures a critical mass in specialised areas of expertise. This has helped our clinical trials program to grow in breadth and depth, particularly in oncology. Two new collaborative groups — COGNO (neuro-oncology) (p. 17) and PC4 (primary care) (p. 19) — have started to work with the support of the CTC.

We are doing more multimodal studies, including trials of chemotherapy with biologicals in addition to radiotherapy and, or, surgery. Recent examples are TOPGEAR, ALaCaRT, and SUPER (p. 44), which have brought additional challenges to the program. Where possible, trials include consent for tissue analysis, so that molecular and genetic studies can be an integral part of the trials (p. 41).

Much of this new work has been underpinned by repeated successful infrastructure grants from Cancer Australia and the Cancer Institute of NSW. The CTC, with the oncology collaborative groups, was awarded three Cancer Institute infrastructure grants, one which is supporting central generic processes and systems, specifically in the areas of data systems, biostatistics and quality assurance. Two other grants support infrastructure positions for each of our collaborative groups.

The Clinical Trials Development Unit, supported by a grant from Cancer Australia to the CTC and the Centre for Biostatistics and Clinical Trials at Peter MacCallum Cancer Centre, was an initiative to move towards formally standardising the conduct of oncology studies in Australia and New Zealand.

The neonatal program is also expanding, with the aid of an NHMRC grant for the Australian Placental Transfusion Study (p. 22). In cardiovascular disease, ASPIRE (p. 26) is expanding internationally. The CTC’s two largest and longest trials, LIPID (p. 26) and FIELD (p. 24), are still in long-term follow-up. Important clinical and biomarker substudies for both trials are in preparation or publication.

“Much of our growth and new work has been underpinned by successful infrastructure grants.”
Wendy Hague, clinical trials program director
The oncology group at the CTC specialises in running phase II and phase III investigator-initiated trials, from concept development to final manuscript preparation and every step in between. The CTC has worked with over 100 clinical sites across Australia and New Zealand as well as in Singapore, Canada, Taiwan and the UK to conduct trials to improve outcomes for cancer patients. The trials are run in partnership with specialised collaborative groups. Five well-established groups operate through the CTC:

- Australasian Gastro-Intestinal Trials Group (AGITG)
- Australia New Zealand Gynaecological Oncology Group (ANZGOG)
- Australasian Lung Trials Group (ALTG)
- Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP), formed from a merger in 2008 of the Australian and New Zealand Germ Cell Trials Group and the Australian Prostate and Urogenital Cancer Group
- Cooperative Trials Group for Neuro-Oncology (COGNO).

The CTC also works closely with:

- Australian New Zealand Breast Cancer Trials Group (ANZ BCTG), as the central randomisation and statistical centre
- Primary Care Cooperative Cancer Clinical Trials Group (PC4), a diverse group initiating trials requiring innovative methods of design and operation.

These Australian groups, in turn, are associated with large international cancer collaborations, so the CTC remains at the heart of research initiatives throughout the world.

In 2008–2009, 14 trials were actively recruiting and several trials reached important milestones, including activation, final analysis, presentation and reporting.

The oncology group of 45 staff, led by the program manager and the team of associate program managers, have maintained the CTC’s reputation for initiation, concept development, coordination, medical support, timely completion, analysis and reporting of high-quality trials.

At right: Martin Stockler, oncology co-director and oncology managers
Breast cancer

Australian New Zealand Breast Cancer Trials Group

The CTC is randomisation and statistical centre for the Australian New Zealand Breast Cancer Trials Group (ANZ BCTG).

The group’s breast cancer trials are coordinated at the operations office based in Newcastle. The CTC registers and randomises the trial patients and also undertakes statistical and other analyses of trial data. The ANZ BCTG has 13 studies open to recruitment; the CTC randomised 886 patients during 2008–2009.

www.anzbctg.org

SNAC 2: multicentre trial of sentinel node biopsy for early breast cancer

Before the SNAC trial, women with early breast cancer routinely had axillary clearance (removal of armpit lymph nodes) to assess the spread of their disease. The first-year follow-up of SNAC patients published in 2009 showed that in women with tumours smaller than 3 cm, sentinel node biopsy of selected lymph nodes could identify axillary tumours and had fewer side-effects (such as lymphoedema).

In SNAC 2, the investigators are continuing this research by recruiting women with large and multiple tumours as well. The aim is to determine whether the risk of recurrence is greater with the less invasive operation in various subgroups of women. If so, sentinel node biopsy will become standard practice for all women with early breast cancer.

Advanced cancer studies: ‘How long have I got?’

Dr Kiely is a medical oncologist investigating how to estimate survival duration in patients with various types of incurable cancer and how clinicians can communicate this information to patients. In her initial work, she has reviewed data on chemotherapy for metastatic breast cancer that would help clinicians estimate and describe prognosis for their patients in this situation. She and her colleagues have determined a distribution of survival that can be used to show typical, best and worst case scenarios for women starting chemotherapy. One aim of this work is to help clinical oncologists convey realistic hope when discussing life expectancy with patients with advanced cancer.

These studies will extend the value of data obtained from the CTC’s oncology trials to provide new information and prognosis tools for practising clinicians.

Belinda Kiely was awarded a National Breast Cancer Foundation doctoral fellowship for her studies in advanced cancer.
Gastrointestinal cancer trials

The CTC coordinates the trials of the Australasian Gastro-Intestinal Trials Group (AGITG), the Australian collaborative group for research into gastrointestinal cancers (which can occur in the oesophagus, stomach, liver, gall bladder, pancreas or bowel).

The CTC works closely with AGITG clinicians and:
- provides project management, trial coordination, quality assurance, trial design, biostatistical analysis and data management
- supports new trials, including multidisciplinary trials in surgery, radiotherapy, chemotherapy, translational research and supportive care
- educates and trains new investigators and research fellows in trial methods and protocol development

Throughout 2009, the CTC managed and coordinated 25 trials in gastrointestinal cancer, some in the final stages of development, some actively recruiting and some in follow-up.

Over 2700 patients have now been recruited to 38 AGITG trials, and the group has 75 sites in Australia, New Zealand, Singapore, Hong Kong and the United Kingdom. In 2008–2009, five trials were open to recruitment — CO20, QUASAR2, DECO, REGISTER and PETACC 6. Da Vinci, ESPAC3 and Adjuvant GIST closed during 2009, and another 7 trials were in active follow-up.

www.gicancer.org.au

MAX STUDY—a low-toxicity regimen for colorectal cancer

Analysis of the MAX study data was completed. The results showed that adding bevacizumab, with or without mitomycin, to capecitabine significantly improves progression-free survival without causing major additional toxicity or impairment of quality of life. This new low-toxicity regimen may be a treatment option for patients with metastatic colorectal cancer, especially older patients.

The results of MAX were presented at the meeting of the American Society of Clinical Oncology and at the European Multidisciplinary Cancer Congress in 2009.

‘For an associate oncology program manager at the CTC, no two days are alike. At one moment I am working with leading Australian researchers developing new studies which could potentially change the standard of care for a particular disease and the next I’m involved in coordinating and managing the talents of our clinical trials team, pointing them towards a common goal. Due to the sheer length of our trials, seeing a project through from its infancy to completion is a rare feat. However, being involved in the daily challenges allows us to use our diverse range of skills and knowledge leading to achievement of our professional goals.’

— Reena Gill, associate oncology program manager for the Australasian Gastro-Intestinal Trials Group

MAX STUDY—a low-toxicity regimen for colorectal cancer
The CTC coordinates all the trials of the Australia New Zealand Gynaecological Oncology Group (ANZGOG), which was established in 2002 and incorporated in 2009. ANZGOG collaborates with international study groups through membership of the Gynecologic Cancer Intergroup (GCIG). The associate oncology program manager for the ANZGOG trials, Julie Martyn, recently became chair of its Harmonisation and Statistics Committee.

ANZGOG has recruited over 500 patients from 47 clinical sites in Australia and New Zealand. Currently, three are open to recruitment: PORTEC 3, OVAR 16 and Symptom Benefit. ICON 6 (stage 2) and Outback are pending. Another six trials, in ovarian cancer, have closed to recruitment, and their patients are being followed up.

The CTC is statistical centre for the large international Calypso trial. This ovarian cancer trial showed that combination treatment with carboplatin and pegylated liposomal doxorubicin led to longer progression-free survival than standard chemotherapy in patients with platinum-sensitive recurrent ovarian cancer. The results were presented at the meeting of the American Society of Clinical Oncology, the European Society of Gynecological Oncology and the European Society for Medical Oncology in 2009. Patients continue to be followed up, and work on secondary analyses is continuing.

www.anzgog.org.au
Genitourinary cancer trials

In 2008, the Australian and New Zealand Germ Cell Trials Group (ANZGCTG) and Australian Prostate and Urogenital Cancer Group (APUG) amalgamated to form the new collaborative group, the Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP). ANZUP is supported by funding from Cancer Australia under its Support for Cancer Clinical Trials program.

SORCE, an international trial initiated in the UK and Europe, is the first ANZUP trial in renal cell cancer, and began in Australia in 2009. Australian investigators, Martin Stockler and Prunella Blinman, have also designed and developed a substudy on patient preferences (page 18).

Accelerated BEP, a feasibility study of an accelerated chemotherapy regimen for advanced germ-cell tumours, continues to recruit patients. Encouraging results from this trial and a similar UK trial have provided the rationale for a full-scale randomised trial of the regimen. Chemo & Cognition is a national longitudinal study of learning, memory and attention after chemotherapy for testicular cancer. The study will have implications for informed consent and the way future clinical trials are investigated, and is especially important with cancer survivors living longer. Another trial is seeking to establish the value of an aprepitant-containing anti-emetic regimen in preventing chemotherapy-induced nausea and vomiting for patients receiving 5-day cisplatin-based chemotherapy.

Eligible patients can enrol in all three trials: Accelerated BEP, Aprepitant and Chemo & Cognition.

www.anzup.org.au

Brain cancer trials

The Cooperative trials Group for Neuro-Oncology (COGNO) is a national collaborative trials group formed in late 2007 with funding from Cancer Australia.

The CTC is the coordinating centre for the group and is currently completing data management for a phase II trial of the combination of temozolomide and liposomal doxorubicin for glioblastoma multiforme, a brain cancer.

The group has also joined with the European Organisation for Research and Treatment of Cancer (EORTC) to conduct the CATNON trial in Australia. The trial is investigating chemotherapy treatment added to radiotherapy for glioma. COGNO held its first scientific meeting in 2008 and discussed three new local concepts for trials to add to those already running and two being prepared for start-up.

www.cogno.org.au

ANZUP IS OFF TO A GOOD START

In 2009, ANZUP continued to recruit patients to five trials and activated another — RAVES, in collaboration with the Trans-Tasman Oncology Group.

‘The associate oncology program manager’s role for ANZUP at the CTC has provided me with opportunities to mentor more junior staff, liaise with experts in the field, and gain exposure to all aspects of project management from concept development to close-out. The opportunities offered by CTC are diverse, and both personally and professionally rewarding.’

— Amy Boland, associate oncology program manager for the Australian and New Zealand Urogenital and Prostate Cancer Trials Group
INDIVIDUAL PATIENT PREFERENCES IS A MAJOR STRAND OF THE CTC’S ONCOLOGY RESEARCH

Dr Blinman is undertaking studies on the preferences of patients and their doctors for chemotherapy treatment. The studies use the methods of Simes and Coaste to determine how patients and doctors trade off the benefits and harms of chemotherapy.

In a recently published study, she found that very small survival benefits made adjuvant chemotherapy for early colon cancer worthwhile, but preferences were highly variable and not readily predictable.

Dr Blinman received a Young Investigator Award from the ASCO Cancer Foundation in the United States for her work on preferences for adjuvant chemotherapy in non-small-cell lung cancer. She presented results at national and international meetings in 2009, and this work is continuing.

Other preferences studies include one determining preferences for adjuvant sorafenib in resected renal cell cancer. This is a longitudinal preference study developed, coordinated and led by the CTC as part of the international phase III SORCE trial (page 46).
Lung cancer trials

The CTC coordinates the trials of the Australasian Lung Cancer Trials Group (ALTG), which aims to reduce the incidence and related mortality and morbidity of lung and thoracic cancers and improve the quality of life of patients with lung cancer. The group is supported by infrastructure grants from Cancer Australia.

Four trials have been developed: MATES, NITRO, PACT in non-small-cell lung cancer, and BR.29. MATES, a study of thalidomide for mesothelioma, is a collaboration with a Dutch group, and BR.29 is a collaboration with the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG). A trial using a novel vascular disrupting agent for mesothelioma is being developed.

‘Preferences for adjuvant chemotherapy in non-small-cell lung cancer: what makes it worthwhile to patients and their doctors?’ is a multicentre observational cohort study of preferences for adjuvant chemotherapy for patients undergoing surgery for lung cancer. Results for patients’ preferences were presented at the World Conference on Lung Cancer in 2009 by CTC research fellow, Prunella Blinman.

www.altg.com.au

An initiative to close the evidence gaps in oncology in primary care

In mid-2009 the CTC began collaborating with the Primary Care Cooperative Cancer Clinical Trials Group (PC4), the newest national cooperative oncology group funded by Cancer Australia.

The group focuses on prevention and detection of cancer and care of people with cancer and currently unanswered research questions in these areas. It is actively working to develop and conduct large-scale multisite studies and build research infrastructure in primary care.

The CTC has representation on executive and advisory committees, and its particular roles are trials development support, with advice and expertise in trial operations, statistics and clinical epidemiology. In 2009, the CTC worked with the group to run two concept-development workshops, where participants had an opportunity to workshop their ideas for new clinical trials.

A new approach to trials research in primary care is needed. It has special challenges, including the diversity of general practice patients and the complexity of their care, and the variety of health professionals involved.

www.pc4tg.com.au
Neonatal trials

The CTC started its first neonatal trial in 2001 as part of its aim of conducting trials in areas of need. The trial, INIS, now approaches completion after enrolling over 3400 infants internationally.

Other large trials are being conducted or developed — such as BOOST II, which will soon reach full recruitment, and APTS, which began as a pilot study in 2009. These trials also contribute to worldwide meta-analyses of data from many thousands of patients. The CTC has participated or taken a lead in setting up networks of investigators who are making this happen.

What level of oxygen is right for premature babies?

The CTC’s BOOST II trial (Benefits of Oxygen Saturation Targeting) is one of several large trials around the world aiming to ascertain which of two ranges of oxygen saturation within the current clinical range used is better for very premature babies.

Lucille Sebastian, INIS manager, and Alpana Ghadge, BOOST II manager.
Too little oxygen for long periods may harm brain cells and contribute to chronic lung disease or increase the risk of death. Too much oxygen for long periods is known to cause damage to the eyes, may impair brain development or lung development, and may also increase the risk of death.

Infants are randomised to either 85–89% oxygen saturation target or to 91–95% oxygen saturation target. Oxygen saturation is measured with adjusted, masked Masimo Radical SET pulse oximeters. The oxygen saturation monitoring for the study continues until the infant reaches a corrected gestational age of 36 weeks or consistently breathes in room air.

Of the 1036 infants enrolled, 218 have been followed up for their outcomes at 2 years, corrected for gestation.

The abnormalities being measured are rare, so even 1200 infants in the trial will not be enough to determine a clear difference between the two oxygen targets. The data from the trial are being combined with data from five other similar trials in other countries in the international Neonatal Oxygenation Prospective Meta-analysis (NeOProM) (page 32). Eventually, data from 5200 infants will be available for a meta-analysis that was planned before the trials began.
Immunoglobulin for infection

The International Neonatal Immunotherapy Study (iniS) is evaluating polyclonal immunoglobulin (IVIG) added to antibiotic therapy for newborn infants with serious infection. Infants were recruited from Australia, New Zealand, United Kingdom, Europe and Argentina.

Infants with low birth weight and suspected serious infection received infusions of IVIG (Intragam®) or placebo. The main outcome being measured is survival without major disability at 2 years, corrected for gestational age. iniS finished recruitment in May 2007 in Australia and New Zealand. The cohort of 1398 babies from Australia and New Zealand was 40% of the global total of 3493. Locally, the trial successfully followed up 97% of babies eligible to answer the primary study question.

Does placental blood help premature babies?

Researchers led by Professor William Tarnow-Mordi are investigating the value of a simple technique to improve the health and survival of infants born more than 10 weeks early. These infants have a higher rate of death and disability than babies born at term.

Placental transfusion can deliver as much as 30 more millilitres of blood to the baby. It is done by one of three methods: cord milking, delayed cord clamping, or a combination of both. The method leading to the highest haemoglobin levels will be the intervention arm in the main trial. Recruitment began in 2009 for the pilot study.
“Amputation is a real threat for diabetes patients. Fenofibrate treatment appears to substantially reduce this risk”

Anthony Keech, deputy director
Cardiovascular trials

The international FIELD trial: results continue to reveal benefits of treatment for diabetes

The FIELD (Fenofibrate Intervention and Event Lowering in Diabetes) trial is a study of using fenofibrate to modify blood lipids and therefore reduce cardiovascular disease in people with type 2 diabetes.

The main results were published in 2005, but subsidiary analyses looking at secondary and tertiary endpoints planned in the trial protocol are still continuing. One study showed that fenofibrate reduced the risk of amputation of the toes by almost half. Another explored various features of the metabolic syndrome: people with very high triglyceride levels had the highest risk and also the greatest benefit from fenofibrate treatment.

Many patients in FIELD started using statin drugs during the 5 years of the trial, confounding the main results. The investigators therefore developed a new method for adjusting the effects of a study drug for other treatments taken up during a trial. This was presented at the meeting of the American Heart Association.

DIABETIC MICROVASCULAR DISEASE

Dr Ting is looking at the safety of fenofibrate and its effects on diabetic kidney disease. The well-known acute rise in serum creatinine with fenofibrate has been found to be completely reversible even after 5 years of treatment. Hence, the creatinine rise may not indicate structural damage to the kidney; in fact, the preservation of renal function is unmasked on drug withdrawal.

Part of the project examines risk predictors of diabetic microvascular disease, with emphasis on renal pathology. The loss of glomerular filtration and albumin leak appear to represent two separate pathological processes with different sets of risk factors.

Complementary basic science experiments investigate the mechanism of action of fenofibrate. Mesangial, podocyte and proximal tubule cell cultures will be exposed to a diabetic milieu, and the effects of fenofibric acid on the pathological changes of diabetic nephropathy examined: for example, upregulation of collagen. Animal experiments will be conducted to validate these findings, and PPAR-alpha knockout mice will be used to find out whether the renal effects of fenofibrate are solely PPAR-mediated or not.
Over a million Australians have diabetes. The costs of diabetes were estimated by the Diabcost survey in 2002 at $3 billion a year, and diabetes is implicated in 8% of deaths in Australia. Therefore, the research by the FIELD investigators has important financial implications, especially with the increased cost of health care and the aging population.

The next major phase of the FIELD trial is laboratory analysis of patients’ blood samples. This will allow the investigators to determine biological and genetic markers of risk. FIELD is also continuing with long-term follow-up. Of about 8000 patients in Australia and New Zealand, about 16% have died and the rest are being followed up by questionnaire or registry search to ascertain their outcomes.

PHD

LABORATORY AND CLINICAL VASCULAR STUDIES

Dr Rajamani is using cell, molecular, and animal models and human clinical studies to determine the mechanisms of blood vessel damage and repair in patients with type 2 diabetes. These studies are extending the results of the FIELD trial. The objective is to identify novel mechanisms of vascular injury in diabetes and potential pathways through which the clinical benefits of fenofibrate are mediated — at genetic, cellular and molecular levels.

In 2009, Dr Rajamani took a major role in the FIELD amputation study, published in The Lancet. Current research includes:

- using clinical and biochemical variables to predict the risk of an amputation
- laboratory studies of the effects of hyperglycaemia on migration, proliferation, tubulogenesis and apoptosis of cultured human vascular endothelial cells
- simulation of limb ischaemia, wound healing and the effects of fenofibrate in mice
- finding specific genetic biomarkers of vascular injury in diabetes patients.

Kushwin Rajamani, cardiology fellow

FIELD AMPUTATION STUDY

An amputation due to diabetes occurs around every 30 seconds somewhere in the world.

In FIELD, fenofibrate treatment was found to reduce the risk of a first diabetes-related amputation by 36%. This important finding was reported in The Lancet in May 2009. The risk of a minor amputation (toes) without known large-vessel disease was 47% lower in the fenofibrate group.

A patient’s height was a major predictor of amputations. The risk of an amputation increased by 60% for every 10 centimetres of a patient’s height.

Amputation is a real threat for diabetes patients, even when their blood glucose and blood pressure are kept under control, and is dramatically higher for those who have already had skin ulceration or amputation. Fenofibrate treatment appears to substantially reduce this risk.
A large cost-efficient trial: ASPIRE

Several million patients worldwide who have had a venous thromboembolism are at risk of another.

The aim of ASPIRE is to determine whether low-dose aspirin prevents recurrence of thromboembolism. ASPIRE is also examining the safety of long-term aspirin in these patients, exploring risk factors for recurrent thromboembolism, exploring the link between venous and arterial thrombosis, and assessing the cost-effectiveness of aspirin therapy.

ASPIRE began in Australia and New Zealand in 2004. A larger patient base was sought by expanding into Singapore, the United Kingdom, more recently, India and, in the future, Argentina. Over 650 patients have been recruited.

Italy has a very similar trial (WARFASA). The ASPIRE and WARFASA investigators are cooperating in the INSPIRE prospective meta-analysis, led by the Australian investigators.

Long-term effects of cholesterol-lowering therapy: LIPID

Patients in the Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) trial were recruited between 1990 and 1992 and had clinical follow-up for an average of six years. The results of the trial were published in 1998. Over 90% of surviving patients are still being followed up by letter and telephone, and other data come from searches of registers of morbidity, mortality and cancer. The information is being used to assess the long-term safety and cost-effectiveness of pravastatin treatment, a project funded by the NHMRC.

Blood samples collected over the first six years of the trial are being analysed in the laboratories of collaborating scientists from Germany, Sweden and the United States, and will soon be used in a new round of investigations of how various blood components are related to, first, the risk of disease and, second, the effects of pravastatin.

Recent publications resulting from LIPID data include: biostatistical studies analysing the risk of a recurrent cardiovascular event; a study showing that two major biomarkers were associated with future coronary heart disease; a study describing differences in Australian and New Zealand cardiovascular mortality according to socioeconomic status; and an investigation of optimal intervals for cholesterol monitoring.
Coronary heart disease biomarkers

The LIPID study continues to provide information about the ongoing risks of patients who have had coronary heart disease. One study showed that two biomarkers predicted the risk of future cardiovascular events (with odds of more than 1) and two others did not. The analyses were adjusted for confounders (including age, prior myocardial infarction, diabetes, and prior stroke).

Biomarker

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Odds ratio with 95% CI</th>
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<tr>
<td>NT-proBNP</td>
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<tr>
<td>TIMP-1</td>
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<td>C-reactive protein</td>
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<td>Interleukin-6</td>
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Helen Pater, project manager for LIPID
Biostatistics

Biostatistics has a central role in trials from initiation and design through to the final report. CTC biostatisticians have responsibility as the statisticians for national and international trial groups undertaking research into cardiovascular disease, diabetes, neonatal intensive care, and breast, gastrointestinal, gynaecological, urogenital and brain cancers. They also participate in independent safety data monitoring committees, which oversee trial safety at arm’s length from the study investigators.

As part of a new collaboration with the Menzies Research Institute in Darwin, in 2008 and 2009 statisticians presented workshops covering material from design of trials to advanced statistical methods for analysis of trial data. Researchers had the opportunity to present a study plan for discussion and development. This activity has paved the way for collaborative trials in Aboriginal health. The first of these, ABRACADABRA, is a multisite trial to assess a web-based early literacy program. School absenteeism has presented special challenges. The success of the intervention will be measured by improvements in students’ phonological awareness and word reading. Other outcomes to be assessed include early literacy skills, phoneme–grapheme correspondence and mathematics. Poor literacy underpins many health problems in indigenous groups, so an improvement in early literacy can potentially improve health in the future.

PHD

STATISTICAL METHODS AND ISSUES IN ANALYSIS OF HEALTH-RELATED TRADE-OFFS

Overall summary measures are often needed in clinical trials that evaluate quality of life, in order to encapsulate the balance of positive and negative impacts of conditions and treatments on different quality-of-life dimensions and on other outcomes such as health status and survival.

In this project, Dr Annette Kifley and colleagues are developing joint models for multidimensional, mixed outcomes in quality-of-life trials by applying and extending latent variable modelling methods. The work will be useful for pharmacoeconomic assessments and individual clinical decision making about the overall value of different therapeutic strategies.
“Biostatistics plays a pivotal role in underpinning the science of clinical trial designs as well as ensuring the study results are correctly interpreted.”

Val Gebski, director, Biostatistics.

DEVELOPING A NEW CLINICAL TRIAL: THE STATISTICIAN’S VIEW

‘In the Mel-D study, a phase II pilot trial to assess the effectiveness of vitamin D in preventing melanoma recurrence, the design team has included a biochemist, a surgeon, a clinical researcher, a statistician, a clinical trials manager, a data manager and a clinical trials coordinator.

‘It has taken over 1 year from the concept stage to getting the trial up and running. It will take at least another 2 years before the study can answer its research question.

‘My role in the Mel-D trial as a biostatistician is not just about “doing the stats”. It’s about problem solving, learning how to communicate statistical concepts to the group, and helping design case report forms, among other things. It has been insightful and rewarding experience.’

— Diana Zannino, biostatistician
CTC Outreach

CTC Outreach is a research support program designed to promote high-quality clinical trials in currently unsupported clinical areas, including surgery, current clinical practice, new health technologies, clinical management, palliative and supportive care, and complementary medicine. Expertise available to new investigators and groups includes:

- study design and conduct, including statistical considerations, and database and forms design
- concept development, including outlines, trial proposals, protocols and funding applications
- randomisation and drug distribution systems
- development of clinical research skills
- establishing trials support networks in therapeutic areas currently not catered for.

During 2008–2009, Outreach supported over 60 research and education activities. Highlights have included collaboration on several projects funded by the NHMRC and sponsorship of training workshops and short courses in trial concept development and methods. The functionality of the CTC’s randomisation and data management systems have been extended, so more trials can be supported. Outreach has contributed to the development and ongoing success of research networks in kidney disease, paediatrics, neonatal disorders and indigenous health.

The program is funded by the National Health and Medical Research Council of Australia.

www.outreachclinicaltrials.org.au

Biostatistics Collaboration of Australia (BCA)

The BCA, a collaboration of seven universities administered at the CTC, is meeting the workforce need for biostatisticians in Australia. The BCA offers postgraduate qualifications from each of its member universities and provides courses by distance education. After 10 years of its operation, 182 have graduated (86 master, 33 graduate diploma, 63 graduate certificate) and currently 248 students are enrolled.

This achievement as a model for collaborative education was reported in a paper in The American Statistician: ‘Biostatistics @ distance: a model for successful multi-institutional delivery’.

www.bca.edu.au
Education for clinical trials

The CTC has a program of education activities designed to increase the quality and number of trials undertaken in Australia and improve the interpretation and implementation of their results. New courses are continually being developed:

• Time-to-event analysis is an advanced statistical technique accounting for the observation that the clinical event being measured may occur early in some patients and later in others; others yet may die or drop out of a trial for other medical reasons altogether. The intense 5-day course in time-to-event methods was first offered in 2008. Simple and complex analysis strategies were covered, with an emphasis on interpreting results and the advantages and pitfalls of different approaches.

• Equivalence and noninferiority study designs are becoming increasingly common, but design and analysis methods are still not well understood. A course on equivalence designs and interim analysis was presented for the first time in 2009. The participants came from varied backgrounds, mainly medical, with most having a basic level of knowledge. Participants appreciated the quality and comprehensiveness of the course, saying it was pitched at the right level.

• The CTC with Professor James A Talcott from Harvard conducted a 5-day advanced clinical trials course under the auspices of the NSW Office of Scientific and Medical Research and the NSW Cancer Institute. Participants brought their trial proposals for developing in practical sessions.

CTC biostatistians and others develop and deliver regular educational programs, including: short courses for clinical researchers and biostatisticians; lectures and workshops for radiation oncology trainees; workshops on study design and data management for paediatrics at the Children’s Hospital Westmead; and workshops on developing concepts and protocols for trials.
Combining trial evidence

Systematic reviews and meta-analyses

In systematic reviews, information is obtained comprehensively from all possible sources to obtain the best unbiased evidence. The CTC undertakes systematic reviews and meta-analysis to investigate important clinical questions and also to assess new medical devices and technology.

Prospective meta-analysis, in which the data collection and analyses for more than one trial are planned in concert before the trials are conducted, is the gold standard in medical research. It is particularly useful in research areas where large numbers of patients are required for statistical analysis. The CTC is a leader in prospective meta-analysis methods.

Perinatal meta-analyses

**OXYGEN THERAPY FOR NEONATES**

The Neonatal Oxygenation Prospective Meta-Analysis (NeOProM) is a current collaboration of investigators for the CTC’s BOOST II trial (page 21) and trial investigators in the United States, United Kingdom, New Zealand and Canada, who together plan to recruit over 5000 infants born at less than 28 weeks’ gestation. This prospective meta-analysis is expected to answer the question of the optimum level of oxygen for very preterm infants.

**NITRIC OXIDE IN ASSISTED VENTILATION**

Preterm infants often require assisted ventilation, which has a risk of lung and neurological injury. Some trials have shown that inhaled nitric oxide reduces these risks. In MAPPINO, individual-patient data from several trials are being reanalysed to settle this question and to identify any characteristics of the infants that may show benefits of inhaled nitric oxide.

**HIGH-FREQUENCY OSCILLATORY ASSISTED VENTILATION**

Prevention of Ventilator-Induced Lung injury in Preterm Infants with Respiratory Distress Syndrome (PreVILIG) is a systematic review and individual-patient-data meta-analysis of the value of high-frequency oscillatory ventilation compared with conventional mechanical ventilation in reducing the risk of bronchodyplasia and consequent disability in preterm infants. The dataset includes 3229 participants in 10 trials.
The CTC undertakes systematic reviews and meta-analysis to investigate important clinical questions and to assess new medical devices and technology.

Dr Lisa Askie, director of systematic reviews. Lisa also has leading roles in international neonatal collaborations.

ANTIPLATELETS FOR PREVENTING PRE-ECLAMPSIA

The PARIS collaboration was the first individual-patient-data analysis in the perinatal field. It showed that use of antiplatelet drugs, such as aspirin, in pregnancy reduced the risk of pre-eclampsia and other adverse outcomes of pregnancy.

In 2009, Lisa Askie was awarded a research grant from the UK Medical Research Council for further methodological research using the PARIS dataset.
Cardiovascular disease meta-analyses

INTERNATIONAL TRIALS OF CHOLESTEROL-LOWERING DRUGS
The Cholesterol Treatment Trialists’ (CTT) Collaboration was the first international prospective meta-analysis group, established in 1994 as a way of pooling individual-patient data from many trials to answer research questions about the effects of the cholesterol-lowering statin drugs. The analysis of data from the subgroup of patients with diabetes (in 14 trials with over 8000 vascular events) was published in 2008. This confirmed that statin therapy reduced the risk of heart disease mortality in people with diabetes at risk of vascular disease.

Data from 25 trials of statins compared with a control or high-dose compared with low-dose statins are now available. These patients had almost 25,000 vascular events, such a large number that analyses of many subgroups can be done with statistical precision.

ASPIRIN TO PREVENT RECURRENT VENOUS THROMBOEMBOLISM?
The investigators of ASPIRE (page 26) are collaborating with the investigators of the WARFASA study (initiated in Italy) in INSPIRE, a prospectively designed meta-analysis of individual patient data. The two groups harmonised their protocols to allow a prospective meta-analysis to be done. The study aims to determine whether aspirin reduces the risk of recurrent thromboembolism.

ACUTE CORONARY HEART DISEASE
An individual-patient-data overview of immediate coronary angioplasty or thrombolysis for the treatment of acute myocardial infarction has shown the benefits of angioplasty and the importance of a comprehensive, unified approach to delivery of cardiac care.

VIGOUR COLLABORATION:
INTERNATIONAL CARDIOVASCULAR RESEARCH SINCE 1990
Data from the 1990s GUSTO trials of acute myocardial infarction continue to be analysed. A study of nearly 50,000 patients comparing the acute mortality and bleeding risks associated with 162 mg versus 325 mg aspirin showed that a lower dose of aspirin is as effective as the higher recommended dose for patients with ST-elevation myocardial infarction.

A collaborative study of 136,247 patients in GUSTO trials and other trials of the VIGOUR collaboration investigated the relationship between the sex of the patient and mortality in the 30 days after they presented at hospital for myocardial infarction or unstable angina. Women had a higher risk of death than men, but were on average older and had more risk factors, which explained most of the differences. The study highlighted the differences between men and women presenting to hospital for acute heart disease.
Reviews of evidence in the Cochrane Library

The Cochrane Library publishes systematic reviews of the evidence in many fields of health care, which is made possible by specialist groups around the world that prepare, maintain and peer-review these studies and protocols for studies.

The CTC is the editorial base of the Cochrane Breast Cancer Group, which has infrastructure support from the Australian Department of Health and Ageing. The group coordinates the Cochrane reviews on breast cancer and maintains a specialised register of over 7000 references. A current project is design of a search portal to broaden public access to breast cancer data. The group has facilitated the publication of 38 reviews and has 15 reviews in progress. CTC members of the group have published reviews themselves, most recently one on radiotherapy for ductal carcinoma and another on single-agent compared with combined chemotherapy regimens for metastatic breast cancer.

CTC authors also write systematic reviews for the Cochrane Library on other topics. In 2009, two systematic reviews of evidence on treatments for preterm infants were published.

Fergus Tai, Cochrane Breast Cancer Review Group trials search coordinator
Evidence from clinical trials

The Australian New Zealand Clinical Trials Registry

The Australian New Zealand Clinical Trials Registry (ANZCTR) provides public data on trials being conducted in Australia, New Zealand, the neighbouring region, as well as some trials from other countries.

The number of trials registered has grown to 3657 since it started in 2005. An average of 90 new trials are submitted for registration each month, an increase from the 2007 average of 54. About 17% have a commercial sponsor.

The ANZCTR is a primary registry in the World Health Organization’s Registry Network, the portal for registered trials throughout the world. The WHO has recently introduced universal trial numbers (UTNs) to enable trials to be tracked more easily. Registry manager Lisa Askie represents the ANZCTR on the WHO platform’s Best Practice Group, which is working to further develop minimal acceptable standards for registries throughout the world.

Worldwide trial search through the WHO portal: http://apps.who.int/trialsearch

Lukas Staub and Sally Lord

DIVERSITY IN WORKING FOR THE AUSTRALIAN TRIALS REGISTRY AND CTC SYSTEMATIC REVIEWS

An objective of the Australian New Zealand Clinical Trials Registry (ANZCTR) is to reduce bias in medical evidence.

‘In my role as a systematic reviews project officer I promote and implement prospective clinical trial registration through the ANZCTR. By creating a public record of clinical trial information, our registry aims to make health information more accessible and transparent. This will ultimately strengthen the efficacy, validity and value of the medical evidence base used to inform health care decisions.

‘I am also involved in various research projects spanning preterm infant health, prospective meta-analysis methods, and obesity in children. The diversity of my role enables me to broaden my knowledge and keep up to date with the latest research being conducted across the full spectrum of health.’

— Kylie Hunter, systematic reviews project officer
Evaluating clinical tests

In clinical medicine, tests are used for diagnosis and prognosis, and to predict the outcome of treatments. Whether a test is known to be accurate is not enough to recommend its use if there is uncertainty about the effects of treatment. When new tests are introduced, the benefit of detection must be weighed against the risks of overinvesigation and overtreatment due to possible misdiagnosis. Evaluation of tests is a major research strand of the CTC's systematic reviews group.

Knowing whether a test plus treatment will improve outcomes requires evidence. The best evidence comes from clinical trials. However, long-term trials may not always be necessary. Sally Lord and colleagues have been investigating the type of comparative evidence needed for test evaluation. They use a flow diagram of a hypothetical randomised trial and focus on specific populations and outcomes where the new-test pathway differs from the standard-test pathway.

Sally Lord presented an invited white paper for the US Agency for Health Care Research and Quality at the launch of the Diagnostic Test Evaluation Work Group, which is developing guidance for conducting comparative-effectiveness reviews of diagnostic technologies.

NEW METHODS FOR EVALUATING DIAGNOSTIC TESTS

The clinical value of a new diagnostic test is ideally assessed by randomised controlled trials that measure its effect on health outcomes. This evidence is rarely available, and test accuracy is often used as a surrogate. However, accuracy can only be estimated if a reference standard is available, and improved accuracy does not necessarily lead to better health for the patient.

In the absence of an accepted reference standard, information that goes beyond ‘classical’ test accuracy can be used in the evaluation of a new test. In collaboration with spine surgeons, Dr Staub and colleagues designed a study to measure the clinical validity of the so-called nerve root sedimentation sign, which uses imaging for diagnosis of lumbar spinal stenosis.

Measuring associations between test results and their downstream consequences may be the best way to judge the clinical validity of this new test. This approach takes into account the diagnostic pathway in which the test will be used, requiring a common understanding between clinicians and epidemiologists of how to apply the principles of test evaluation to addressing clinical questions about tests.
Reviews of new technologies and procedures to inform decisions about public funding

The CTC has a contract with the Medical Services Advisory Committee (MSAC), which advises the Australian Minister for Health and Ageing on evidence relating to new medical technologies and procedures. CTC staff, with clinical experts, review the evidence and analyse the findings relating to safety, effectiveness and cost-effectiveness.

Nine of these reviews were completed in 2008–2009. Six of these were on positron emission tomography (PET), which images physiological function and metabolism, complementing anatomical information from computed tomography or magnetic resonance imaging. PET can detect or exclude various cancers and other pathological processes. The other reviews related to ocular coherence tomography (an imaging technique for retinal eye diseases) and tests for cervical cancer.

Samara Lewis, project manager for MSAC reviews

Luke Marinovich, Sally Worthley and Stephanie Schoeppe
Every patient is different

In clinical trials, usually the benefits and harms of a new treatment are measured as the average for the patient group, but individual patients differ. Trial data are now being used to predict how the course of a disease differs among patients (prognosis) and how patients will respond individually to treatments (prediction). Some prognostic and predictive factors are: risks according to biology; lifestyle risks; and attitudes and values.

Patients may therefore be interviewed about their health or quality of life or asked to allow their blood samples to be analysed. When the data are analysed as part of a trial, the results help clinicians to make appropriate decisions for individual patients.

Risk models in cancer and cardiovascular disease

The data from large numbers of patients in the CTC’s clinical trials are used to calculate the risk of various outcomes in comparable populations.

Clinical measures and genetic and biomarker information, individually or together, may be correlated with patient outcomes to define the risk of an individual patient and the degree of benefit an individual patient might have from treatment. Data from trials has been used to build risk models in cancer and cardiovascular disease.

A substudy of FIELD (page 24) showed that self-reported health on a pen-and-paper scale predicted which patients were at higher risk of major complications of diabetes. A 10-point difference in score classified later risk better than a 1-unit change in the the total cholesterol-to-HDL cholesterol ratio or a 10-year longer duration of diabetes. FIELD data have also been used in models that predict the risk of microvascular disease, such as amputations, kidney disease and diabetic eye disease.

PHD

CAN SURVIVAL AND TREATMENT BENEFIT BE PREDICTED FOR INDIVIDUAL PATIENTS?

Dr Lee’s objective is to develop and test new methods of analysing data from past trials of breast, colorectal and ovarian cancer to assess how molecular biomarkers and other disease and patient characteristics might predict survival and treatment benefit.

He is also examining the role of quality of life in predicting response, toxicity and treatment benefit in advanced breast cancer patients.

Another study involves constructing a risk model that classifies patients into high-, medium- and low-risk in terms of prognosis. This has value for individualising treatment decisions and for future stratification of patients in randomised studies.

Various hypotheses have arisen from the completed Calypso trial of ovarian cancer. These include considering CA125, a biological marker, as a surrogate for treatment efficacy and for identifying groups of patients with different prognosis.
Quality of life information is important for clinical decisions

One way that CTC researchers make the most of trial evidence is by incorporating patient-oriented outcome measures, such as quality-of-life, in trials where possible. Recently published studies have focused on novel ways of measuring quality of life and explored relationships between quality of life and survival.

The Patient Disease and Treatment Assessment Form was designed at the CTC to be a simple, pragmatic measure of health-related quality of life in people with advanced cancer. It was validated by Anna Nowak and colleagues in a substudy of a hepatocellular carcinoma treatment trial. In another substudy, Corona Gainford and colleagues adapted and translated it for use in Taiwan.

Individual wellbeing at the start of treatment has also been studied. For example, in a study by Lee and colleagues, a good score on physical wellbeing and appetite at baseline predicted longer survival in women with advanced breast cancer treated with chemotherapy.

**DERIVING PATIENT-VALUED UTILITIES FROM QUALITY OF LIFE QUESTIONNAIRES TO IMPROVE CLINICAL DECISION MAKING**

Dr Grimison used data from a simple, self-rated, disease-specific questionnaire in three breast cancer trials to create a utility index based on cancer patients’ preferences.

The index can be used to generate utility scores and quality-adjusted life years in clinical trials.

The aim was to facilitate the integration of data about health-related quality of life with traditional trial endpoints (such as survival and tumour response) and ultimately help patients, clinicians and funders make better decisions about cancer treatments, by considering the potential trade-offs between survival and quality of life.
Translational research

Translational research, often described as ‘from bench to bedside’ is the application of laboratory research to patient care. Typically, samples of blood or tumour tissue are collected and analysed for markers that correlate with clinical outcomes. Biomarkers may forecast survival or predict the response of a patient to a treatment — an important part of personalised medicine.

At the CTC, so far about a quarter of trials include an option for patients to consent to biological samples being used in research or being banked for future research. Genetic testing of tissues forms part of the process of screening potential patients for recruitment to some trials. Linking biological and clinical data from a trial creates a powerful data set.

In 2009, Sonia Yip was appointed research fellow and oncology translational research manager. Translational research is also being done in the CTC’s large cardiovascular trials, FIELD (page 24) and LIPID (page 26).

The CTC and its collaborative groups aim to build translational research into their trials where possible, with the aim of future applications at the bedside.

Which patients benefit from targeted chemotherapy for colorectal cancer?

A secondary study of C0.17 (a trial of cetuximab therapy in advanced colorectal cancer), published in the *New England Journal of Medicine*, showed that patients with a K-ras gene variant did not benefit from cetuximab.

In identifying the group of patients who would not benefit, the study thus relieves future patients of needless treatment and its side-effects.

Sonia Yip, translational research manager
Collaborations

The CTC works with organisations around the world in collaborations that lead to better health outcomes in Australia and internationally. New collaborations are continually sought and then consolidated in research projects benefiting the health of Australians and others.

<table>
<thead>
<tr>
<th>Group</th>
<th>Nature of group</th>
<th>Role or activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMICABLE collaboration</td>
<td>Meta-analysis collaboration: international</td>
<td>Member</td>
</tr>
<tr>
<td>ANZ Germ Cell Tumour Study Group (ANZ GCTG)</td>
<td>Collaborative group for testicular cancer trials: Australia, New Zealand</td>
<td>Coordinating centre</td>
</tr>
<tr>
<td>ASPIRE Study Group</td>
<td>Collaborative group for aspire trial: Australia, New Zealand, United Kingdom, India</td>
<td>Coordinating centre</td>
</tr>
<tr>
<td>Australasian Gastro-Intestinal Trials Group (AGITG)</td>
<td>Collaborative group for gastrointestinal cancer trials: Australia, New Zealand International collaborations: NSABP (USA), ECOG (USA), EDRT (Europe), PETACC (Europe), NCIC CTG (Canada), OCTO (UK)</td>
<td>Coordinating centre</td>
</tr>
<tr>
<td>Australian and New Zealand Urogenital and Prostate Clinical Trials Group (ANZUP)</td>
<td>Collaborative group for cancer of the genitourinary system</td>
<td>Coordinating centre</td>
</tr>
<tr>
<td>Australasian Society of Thrombosis and Haemostasis</td>
<td>Professional group undertaking thrombosis trials: Australia, New Zealand</td>
<td>Coordinating centre</td>
</tr>
<tr>
<td>Australasian Lung Cancer Trials Group (ALTG)</td>
<td>Collaborative group for lung cancer trials International collaborations: NVALT (Netherlands), NCIC CTG (Canada)</td>
<td>Coordinating centre</td>
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<tr>
<td>ANZ Gynaecological Oncology Group (ANZGOG)</td>
<td>Collaborative group for gynaecological cancer trials: Australia, New Zealand International collaborations: Gynecological Cancer Intergroup (GCIG), Gynecologic Oncology Group (GOG)</td>
<td>Coordinating centre</td>
</tr>
<tr>
<td>Australian New Zealand Clinical Trials Registry (ANZCTR)</td>
<td>National register of Australian clinical trials</td>
<td>Coordinating centre</td>
</tr>
<tr>
<td>Australian universities</td>
<td>Members of the Biostatistics Collaboration of Australia</td>
<td>Coordinating centre</td>
</tr>
<tr>
<td>Biostatistics Collaboration of Australia</td>
<td>Collaborative group for biostatistics education: national</td>
<td>Coordinating centre</td>
</tr>
<tr>
<td>Cochrane Collaboration</td>
<td>Collaborative group undertaking systematic reviews of trial evidence: international</td>
<td>Editorial base of the Cochrane Breast Cancer Group, co-convening centre for Prospective Meta-analysis Methods Group</td>
</tr>
<tr>
<td>Cholesterol Treatment Trialists’ (CTT) collaboration</td>
<td>Collaboration of clinical trial groups studying cholesterol treatments: Australia, New Zealand, United Kingdom, United States, Italy</td>
<td>Coordination of meta-analyses in heart disease</td>
</tr>
<tr>
<td>Clinical Trials Development Unit</td>
<td>Joint venture with Peter MacCallum Cancer Institute</td>
<td>Statistical support for cancer trials</td>
</tr>
<tr>
<td>Cooperative Trials Group for Neuro-Oncology (COGNO)</td>
<td>Collaborative group for brain cancer trials</td>
<td>Coordinating centre</td>
</tr>
<tr>
<td>Medical Services Advisory Committee Department of Health and Ageing</td>
<td>Government: Australia</td>
<td>Provide assessments of new technologies and other research services</td>
</tr>
<tr>
<td>Early Prevention of Obesity in Children (EPOC) collaboration</td>
<td>Prospective meta-analysis collaboration: international</td>
<td>Data coordination centre</td>
</tr>
<tr>
<td>European Organisation for Research and Treatment of Cancer (EDRTC)</td>
<td>International collaborative group</td>
<td>Collaborator through Australian groups</td>
</tr>
<tr>
<td>FIELD Study Group</td>
<td>Collaborative group for field diabetes trial: Australia, New Zealand, Finland</td>
<td>Coordinating centre</td>
</tr>
<tr>
<td>Group</td>
<td>Nature of group</td>
<td>Role or activity</td>
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<tr>
<td>Gynaecologic Cancer Intergroup (GCIG)</td>
<td>International collaborative group</td>
<td>Collaborator through ANZGOG</td>
</tr>
<tr>
<td>Gynecologic Oncology Group (GDG)</td>
<td>International collaborative group</td>
<td>Collaborator through ANZGOG</td>
</tr>
<tr>
<td>INIS Study Group</td>
<td>Collaborative group for inis trial: Australia, New Zealand, United Kingdom</td>
<td>Regional coordinating centre</td>
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<tr>
<td>INSPIRE</td>
<td>Meta-analysis: ASPIRE and WARFASA (Italy)</td>
<td>Member</td>
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<tr>
<td>LIPID Study Group</td>
<td>Collaborative group for follow-up and genetic studies of lipid cholesterol-lowering trial: Australia, New Zealand, Germany</td>
<td>Coordinating centre</td>
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<tr>
<td>MAPPINO collaborative group</td>
<td>Meta-analysis collaboration: international</td>
<td>Coordinating centre</td>
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<tr>
<td>Medical Research Council (MRC)</td>
<td>Government: international</td>
<td>Collaborator</td>
</tr>
<tr>
<td>Menzies Research Institute and Charles Darwin University</td>
<td>Research institution: Australia</td>
<td>Collaborator</td>
</tr>
<tr>
<td>National Cancer Institute of Canada Clinical Trials Group (NCIC CTG)</td>
<td>Trials research group: Canada</td>
<td>Collaborator through Australian cancer collaborative groups</td>
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<tr>
<td>National Heart Foundation</td>
<td>Non-government organisation: Australia</td>
<td>Coordinator of the LIPID trial</td>
</tr>
<tr>
<td>National Perinatal Epidemiology Unit (NPUEU), University of Oxford</td>
<td>Research institution: UK</td>
<td>Co-collaborator on the INIS neonatal trial</td>
</tr>
<tr>
<td>National Surgical Adjuvant Breast and Bowel Project (NSABP)</td>
<td>Collaborative group</td>
<td>Collaborator through Australian groups</td>
</tr>
<tr>
<td>NeOProm collaborative group</td>
<td>Prospective meta-analysis collaboration: international</td>
<td>Coordinating centre</td>
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<tr>
<td>NSW Cancer Council</td>
<td>Cancer Epidemiology Research Unit</td>
<td>Collaborator</td>
</tr>
<tr>
<td>NSW Cooperative Oncology Group</td>
<td>Collaborative group: NSW</td>
<td>Coordinating centre for the group</td>
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<tr>
<td>Oxford Clinical Trials Office (OCTO)</td>
<td>Trials research group: UK</td>
<td>Cancer trials</td>
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<td>PARIS collaborative group</td>
<td>Meta-analysis collaboration with representation from many countries</td>
<td>Co-coordinating centre</td>
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<tr>
<td>PeVILIG collaborative group</td>
<td>Meta-analysis collaboration: international</td>
<td>Coordinating centre</td>
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<tr>
<td>Primary Care Cooperative Cancer Clinical Trials Group (PC4)</td>
<td>Collaborative group: Australia</td>
<td>Collaborator through the Clinical Trials Development Unit</td>
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<tr>
<td>Primary Coronary Angioplasty versus Thrombolysis (PCAT)</td>
<td>Meta-analysis collaboration with representation from many countries</td>
<td>Co-coordinating centre</td>
</tr>
<tr>
<td>Prospective Prazoatadim Pooling project</td>
<td>Collaborative group: Australia, New Zealand, United States, Scotland</td>
<td>Coordinating centre</td>
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<tr>
<td>Royal Australasian College of Surgeons (RACS)</td>
<td>Professional society undertaking trials of surgery: Australia and New Zealand</td>
<td>Coordinating the SNAC trial in breast cancer with the RACS</td>
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<tr>
<td>Star Child Health</td>
<td>International collaboration</td>
<td>Member</td>
</tr>
<tr>
<td>SIGOUR group</td>
<td>Collaborative group for trials of heart disease: 40 countries</td>
<td>Data coordinating centre, Asia-Pacific region; international statistical centre (HERO-2 trial)</td>
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</tbody>
</table>
### Current trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breast cancer</strong></td>
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<tr>
<td>SNAC 2: Multicentre randomised trial of sentinel-node biopsy versus axillary clearance</td>
<td>Women with operable breast cancer, stratified by various factors, including age and tumour size</td>
<td>Recruitment target: 1012 Recruitment: 131</td>
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<tr>
<td>NHMRC CTC study</td>
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<tr>
<td><strong>Gastrointestinal cancer</strong></td>
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<tr>
<td><strong>Current trials</strong></td>
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<tr>
<td>CO.20: phase II randomised study of brivanib alaninate + cetuximab versus placebo + cetuximab in metastatic carcinoma (AG0207CR)</td>
<td>Patients with treated metastatic colorectal cancer of K-ras wild type</td>
<td>Recruitment target: 370 Recruitment: 312</td>
</tr>
<tr>
<td>NCIC CTG and AGITG study</td>
<td></td>
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</tr>
<tr>
<td>Quasar 2: phase III study of capecitabine and bevacizumab as adjuvant treatment of colorectal cancer (AG0107CR)</td>
<td>Patients with colon cancer treated by surgery</td>
<td>Recruitment target: 250 Recruitment: 189</td>
</tr>
<tr>
<td>OCTO study</td>
<td></td>
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<tr>
<td>REGISTER: multicentre phase II study of risk evaluation in GIST with selective therapy escalation for response (AG0507GS)</td>
<td>Patients with gastrointestinal stromal tumour not suitable for curative surgery</td>
<td>Recruitment target: 80 Recruitment: 8</td>
</tr>
<tr>
<td>AGITG study</td>
<td></td>
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<tr>
<td>PETACC 6: addition of capecitabine to preoperative oxaliplatin chemotherapy and postoperative oxaliplatin chemotherapy for rectal cancer (AG0107CR)</td>
<td>Patients with locally advanced rectal cancer</td>
<td>Recruitment target: 100 Recruitment: 19</td>
</tr>
<tr>
<td>EORTC study</td>
<td></td>
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</tr>
<tr>
<td>TOP GEAR: randomised phase II–III trial of preoperative chemoradiotherapy versus preoperative chemotherapy for gastric cancer (AG0407GR)</td>
<td>Patients with resectable gastric cancer suitable for these treatments</td>
<td>Recruitment target: 120 (stage 1); 652 (stage 2) Recruitment: 3</td>
</tr>
<tr>
<td>AGITG study</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pending trials</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A la CART: Australasian laparoscopic cancer of the rectum, phase III randomised trial of laparoscopy-assisted resection with open resection (AG0609CS)</td>
<td>Patients with primary rectal cancer</td>
<td>Recruitment target: 470</td>
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<tr>
<td>AGITG study</td>
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<tr>
<td>ATTACHE: Timing of surgery and adjuvant chemotherapy for hepatic metastases from colorectal cancer (AG1209CL)</td>
<td>Patients with colorectal cancer and resectable liver metastases and no extrahepatic disease</td>
<td>Recruitment target: 200</td>
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<tr>
<td>AGITG study</td>
<td></td>
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<tr>
<td>ATTAX 3: Phase II study of docetaxel, cisplatin and fluoropyrimidine with or without panitumumab for oesophagogastric cancer (AG0607OG)</td>
<td>Patients with metastatic or locally recurrent oesophagogastric cancer</td>
<td>Recruitment target: 100</td>
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<tr>
<td>AGITG study</td>
<td></td>
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<tr>
<td>LAP07: randomised multicentre phase III study of gemcitabine with or without chemoradiotherapy and with or without erlotinib for adenocarcinoma of the pancreas (AG0208PS)</td>
<td>Patients with locally advanced adenocarcinoma of the pancreas</td>
<td>Recruitment target: 60</td>
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<tr>
<td>AGITG and GERCOR study</td>
<td></td>
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<tr>
<td>SCOT: Short-course oncology therapy, a study of adjuvant chemotherapy in colorectal cancer (AG0308CR)</td>
<td>Patients with fully resected stage III colorectal cancer</td>
<td>Recruitment target: 225</td>
</tr>
<tr>
<td>AGITG study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SURGIST: Phase III randomised study of surgery of residual disease (AG1008GS)</td>
<td>Patients with metastatic gastrointestinal stromal tumour responding to imatinib mesylate</td>
<td>Recruitment target: 35 (ANZ); 350 (international)</td>
</tr>
<tr>
<td>EORTC study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SUPER: Phase III trial evaluating surgical resection of the primary tumour in metastatic colorectal cancer (AG0109CRS)</td>
<td>Patients with unresectable metastatic colorectal cancer</td>
<td>Recruitment target: 400</td>
</tr>
</tbody>
</table>
Current trials

**Da Vinci:** Phase III trial of irinotecan versus irinotecan + De Gramont schedule 5-fluorouracil and folinic acid for colorectal cancer (AG0103CR) AGITG study

Participants: Patients with treated metastatic colorectal cancer

Status: Recruitment target: 100

Recruitment: 89

**EORTC 62024:** Randomised trial of adjuvant imatinib mesylate (Glivec) versus no further therapy after complete surgery

EORTC study

Participants: Patients with fully resected gastrointestinal stromal tumour

Status: Recruitment: 81

**Gofurtgo:** Phase II study of fixed-dose rate gemcitabine–oxaliplatin with 5-fluorouracil and radiotherapy for pancreatic cancer (AG0503P) AGITG study

Participants: Patients with stage II or stage III adenocarcinoma, no metastatic disease and a life expectancy (excluding cancer) of at least 10 years

Status: Recruitment: 11

**C06:** Oral uracil and tharafox + leucovorin compared with 5-fluorouracil + leucovorin for colon carcinoma

NSABP study

Participants: Patients with stage II or stage III colorectal cancer

Status: Recruitment: 81

**C07:** 5-fluorouracil plus leucovorin compared with oxaliplatin with 5-fluorouracil + for stages II and III carcinoma of the colon NSABP study

Participants: Patients with resected stage II or stage III colon carcinoma

Status: Recruitment: 134

**EORTC 62005:** Phase III study of two different doses of imatinib mesylate for CD117-expressing metastatic or unresectable gastrointestinal stromal tumor

EORTC study

Participants: Patients with metastatic gastrointestinal stromal tumour

Status: Recruitment: 116

**EORTC 40983:** Phase III preoperative and postoperative chemotherapy with oxaliplatin + 5-fluorouracil + leucovorin versus surgery alone for liver metastases of colorectal origin

EORTC Study

Participants: Patients with colon cancer with resectable liver metastases

Status: Recruitment: 35

**ESPAC-3:** European study of adjuvant chemotherapies in resectable pancreatic cancer

ESPAC study

Participants: Patients with operated cancer of the pancreas

Status: Recruitment: 133

Gynaecological cancer

**Current trials**

**PORTEC 3:** Phase III trial comparing concurrent chemoradiation and adjuvant chemotherapy with pelvic radiation alone in high-risk endometrial carcinoma

CGOG and ANZGOG study

Participants: Women with advanced endometrial carcinoma

Status: Recruitment target: 200 (ANZ); 500 (international)

Recruitment: 33 (ANZ); 133 (international)

**Symptom benefit:** Palliative chemotherapy for ovarian cancer

(ANZGOG0701) ANZGOG and PoCoG study

Participants: Women with platinum-resistant epithelial ovarian cancer

Status: Recruitment target: 100

Recruitment: 56

**OVAR 16:** Phase III study of pazopanib versus placebo for epithelial ovarian, fallopian tube or primary peritoneal cancer

ANZGOG study

Participants: Women with stage II–IV ovarian fallopian tube or primary peritoneal cancer that has not progressed after first-line treatment

Status: Recruitment target: 50 (ANZ); 900 (international)

Recruitment: 14 (ANZ)

**Accelerated BEP:** Feasibility study of accelerated BEP as first-line chemotherapy for advanced germ cell tumours (ANZGOG0906, ANZGOG0603) ANZGIP and ANZGOG study

Participants: Women with intermediate and poor-risk advanced germ cell tumours (and selected good-risk tumours)

Status: Recruitment target: 25 (revised to 45 in 2009)

Recruitment: 32

**Pending trials**

**ICON 6:** Placebo-controlled trial of concurrent cediranib and chemotherapy versus chemotherapy alone (stage 2) and of maintenance cediranib versus placebo after concurrent cediranib and chemotherapy (stage 3) ANZGOG study

Participants: Women with platinum-sensitive relapsed ovarian cancer

Status: Recruitment target: 100 (stage 2); 400 (stage 3)
<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outback: Phase III trial of addition of adjuvant chemotherapy to standard chemoradiation as primary treatment for cervical cancer ANZGOG study</td>
<td>Women with locally advanced cervical cancer</td>
<td>Recruitment target: 780</td>
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<tr>
<td>PARAGON: phase II study of anastrozole in gynaecological cancers GOG study</td>
<td>Women with potentially hormone-responsive gynaecological cancers</td>
<td>Recruitment target: 100 (ANZ)</td>
</tr>
</tbody>
</table>

**Trials in follow-up**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRIPOD: Phase II trial of intraperitoneal chemotherapy (ANZGOG0501) ANZGOG study</td>
<td>Women with ovarian and related cancers</td>
<td>Recruitment: 39</td>
</tr>
<tr>
<td>ICON 7: Randomised, two-arm, multicentre GOG trial of adding bevacizumab to standard chemotherapy for epithelial ovarian cancer GOG study</td>
<td>Women with epithelial ovarian cancer who have not received systemic antitumour therapy</td>
<td>Recruitment: 76 (ANZ), 1528 (international)</td>
</tr>
<tr>
<td>SCOTROC 4: Multicentre randomised trial of carboplatin flat dosing vs intrapatient dose escalation in first-line chemotherapy</td>
<td>Women with ovarian, fallopian tube or peritoneal carcinoma who are unsuitable for platinum–taxane therapy</td>
<td>Recruitment: 64</td>
</tr>
<tr>
<td>Tarceva: phase III study of erlotinib versus observation (EORTC 55041)</td>
<td>Women with high-risk stage I or stages II-IV ovarian cancer which has not progressed after platinum chemotherapy</td>
<td>Recruitment: 42</td>
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<tr>
<td>Phase III randomised trial of paclitaxel + carboplatin versus triplet or sequential doublet combinations for epithelial ovarian or primary peritoneal carcinoma (GOG 182)</td>
<td>Women with advanced (stage III or IV) primary ovarian or peritoneal cancer</td>
<td>Recruitment: 183</td>
</tr>
<tr>
<td>Prospective study of risk-reducing salpingo-oophorectomy and longitudinal CA-125 screening among women at increased genetic risk of ovarian cancer (GOG 199)</td>
<td>Women aged &gt;30 at risk of ovarian cancer</td>
<td>Recruitment: 83</td>
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</table>

**Genitourinary cancer**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants</th>
<th>Status</th>
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</thead>
<tbody>
<tr>
<td>Accelerated BEP: Feasibility study of accelerated BEP as first-line chemotherapy for advanced germ cell tumours (ANZGCTG0206, ANZGOG0603) ANZUP and ANZGOG study</td>
<td>Patients with intermediate and poor-risk advanced germ cell tumours (and selected good-risk tumours)</td>
<td>Recruitment target: 25 (revised to 45 in 2009) Recruitment: 32</td>
</tr>
<tr>
<td>Aprepitant for germ cell chemotherapy: phase II multicentre trial of a 7-day aprepitant schedule to prevent chemotherapy-induced nausea and vomiting (ANZGCTG0801) ANZUP study</td>
<td>Patients receiving cisplatin-based chemotherapy for germ cell tumours</td>
<td>Recruitment target: 50 Recruitment: 19</td>
</tr>
<tr>
<td>Chemo &amp; cognition: cognitive function and treatment for testicular cancer (ANZGCTG0106) ANZUP study</td>
<td>Patients being treated and followed up for testicular cancer</td>
<td>Recruitment target: 154 Recruitment: 75</td>
</tr>
<tr>
<td>SORCE: Adjunct sorafenib for renal cell carcinoma MRC (UK) and ANZUP study</td>
<td>Patients with resected renal cell carcinoma at intermediate or high risk of relapse</td>
<td>Recruitment target: 25H (ANZ), 1565 (international) Recruitment: 17 (ANZ)</td>
</tr>
</tbody>
</table>

**Lung cancer**

**Current trials**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>NITRO: Phase III multicentre trial of adding nitroglycerine to first-line chemotherapy for advanced non-small-cell lung cancer ALTG study</td>
<td>Patients with advanced non-small-cell lung cancer</td>
<td>Recruitment target: 500 Recruitment: 35</td>
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<tr>
<td>PACT in NSCLC: Preferences for adjuvant chemotherapy in non-small-cell lung cancer ALTG study</td>
<td>Patients with non-small-cell lung cancer, surgeons and oncologists</td>
<td>Recruitment target: 200 Recruitment: 29</td>
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<tr>
<td>BR.29: Phase III randomised trial of adjuvant cediranib vs placebo with paclitaxel–carboplatin chemotherapy for non-small-cell lung cancer NCIC CTG and ALTG study</td>
<td>Patients with advanced or metastatic non-small-cell lung cancer</td>
<td>Recruitment target: 100 (international) Recruitment: 75 (ANZ) 39 (international)</td>
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**Pending trials**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>BR.26: Phase III trial of PF-804 in patients with incurable, non-small cell lung cancer</td>
<td>Patients with stage IIIIB or IV non-small cell lung cancer</td>
<td>Recruitment target: 720</td>
</tr>
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</table>
### Current Trials

#### Brain Cancer

<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>B2P2M2</td>
<td>Patients with pleural mesothelioma which has progressed after pemetrexed and platinum chemotherapy</td>
<td>Recruitment target: 50</td>
</tr>
<tr>
<td>MATES</td>
<td>Patients with malignant pleural mesothelioma, after first-line chemotherapy</td>
<td>Recruitment: 14 (ANZ), 200 (international)</td>
</tr>
<tr>
<td>NVALT, ALTG study</td>
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</table>

#### LGG

- **Phase III study of primary chemotherapy with temozolomide versus radiotherapy for low-grade glioma** *(TR0G 06 01)*
  - COGNO and TROG study
  - Patients with low-grade glioma, stratified for genetic 1p loss
  - Recruitment target: 699 (international), 100 (ANZ)

#### Phase III study of temozolomide and short-course radiation versus radiation alone for glioblastoma multiforme in elderly patients *(TR0G 08 02)*
  - COGNO and TROG study
  - Elderly patients with new glioblastoma multiforme
  - Recruitment target: 100
  - Recruitment: 24

#### Pending trials

- **CATNON**: Phase III trial of concurrent and adjuvant temozolomide chemotherapy araplastic gloma *(EORTC 26053-22054)*
  - EORTC study
  - Patients with non-1p/19q–deleted araplastic gloma
  - Recruitment target: 100 (ANZ); 748 (international)

- **Cabaret**: Phase II study of carboplatin and bevacizumab in for glioma
  - COGNO study
  - Patients with recurrent grade IV glioblastoma multiforme following radiotherapy and temozolomide chemotherapy
  - Recruitment target: 120

- **Phase II study of acetzolamide plus desamethasone versus desamethasone for cerebral oedema in glioblastoma**
  - COGNO study
  - Patients with glioblastoma requiring new desamethasone or dose increase due to progressive or recurrent disease
  - Recruitment target: 86

- **Phase II study of psycho-educational intervention in patients with primary brain tumour**
  - PoCoG led, COGNO cobadged study
  - Patients with confirmed primary brain tumours
  - Recruitment target: 60

#### Cardiovascular disorders

#### Current trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants</th>
<th>Status</th>
</tr>
</thead>
</table>
| ASPIRE              | People who have had 6 months of treatment with warfarin for a venous thromboembolism | Recruitment target: 2000
  - Recruitment: 657     |

#### Trials in follow-up

<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants</th>
<th>Status</th>
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</thead>
<tbody>
<tr>
<td>FIELD</td>
<td>Patients with type 2 diabetes</td>
<td>Recruitment: 9795</td>
</tr>
<tr>
<td>LIPID</td>
<td>Patients with a history of coronary heart disease</td>
<td>Recruitment: 9014</td>
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</table>

#### Neonatal disorders

#### Current trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants</th>
<th>Status</th>
</tr>
</thead>
</table>
| BOSTIT               | Neonates born before 28 weeks’ gestation                                    | Recruitment target: 1200
  - Recruitment: 846     |
| APTS                 | Neonates born before 30 weeks’ gestation                                     | Recruitment target: 1200
  - Recruitment: 6 (ANZ)  |

#### Trials in follow-up

<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants</th>
<th>Status</th>
</tr>
</thead>
</table>
| INIS                 | Neonates with infection and low birthweight who are taking antibiotics      | Recruitment: 1398 (ANZ), 3493
  - (international)    |
Staff

CTC EXECUTIVE
John Simes, BSc(Med)(hons), MB BS(hons), MD, SM, FRACP, director and senior principal research fellow
Anthony Keech, MB BS, MSc, FRACP, deputy director and principal research fellow
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Seshu Atluri, BE

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Frank Schoenig, administrative assistant
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Carlos Sterling, BEng, MBA, finance officer
Nina Stromqvist, BFA(hons), grants coordinator

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Dr David Bernshaw, ANZGOG
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Dr Alex Boussioutas, AGITG
Dr Alison Brand, ANZGOG
Dr Timothy Brighton, ASPIRE
Dr Ian Campbell, SNAC 2
Professor Christopher Christofi, AGITG
Associate Professor Philip Clarke, Health Economics
Dr Andrew Davidson, NITRO
Associate Professor Ian Davis, ANZUP
Dr Jayesh Desai, REGISTER
Dr Katharine Drummond, COGNO
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Dr John Eikelboom, PREDICT
Dr Jonathan Fawcett, AGITG
Dr Kathryn Field, CABARET
Dr Michael Friedlander, ANZGOG
Professor Alexander Gallus, PREDICT
Dr Davina Gherzi, ANZCTR
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Dr Michelle Grogan, ANZGOG
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Dr Michael Jefford, SCOT
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Professor G Bruce Mann, AGITG
Professor Ian Manschner, HERO-2
Dr Nicole McCarthy, ANZGOG
Dr Sue-Anne Mclachlan, ALTG
Dr Michael Michael, DECO
Dr Linda Milesklin, PORTEC-3
Professor Michael J Millward, ALTG
Dr Jeremy Miller, START
Dr Christopher Milross, ANZGOG
Professor Anna Nowak, CATNON
Professor Andreas Obermair, Oncology
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Professor Lyle Palmer, COGNO
Dr Nicholas J Petrelli, AGITG
Dr Cameron FE Flattell, SUPER
Dr Timothy J Price, AGITG
Professor Michael Quinn, ANZGOG
Dr Kushwin Rajamani, FIELD
Dr David T Ransom, SCOT
Dr Danny Rischin, ANZGOG
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Dr Gail Ryan, COGNO
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Professor William Tarnow-Mordi, neonatal trials
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Dr Ru-Dee Ting, FIELD
Associate Professor Guy Toner, ANZUP
Dr Paul Vasey, ANZGOG
Dr Michell Vaughan, ANZGOG
Dr David G Walker, COGNO
Dr Neil Wetzig, SNAC
Dr Desmond Yip, SCOT
Professor John Zalcberg, AGITG

EXTERNAL COMMITTEES

John Simes
ANZ Breast Cancer Trials Group scientific advisory committee
Aspirin to Prevent Recurrent Venous Thrombo-embolism (ASPIRE) trial management committee (chair)

Australian Gastro-Intestinal Trials Group (AGITG) scientific advisory committee, operations executive committee, MAX trial management committee, Quarar 2 trial management committee, Da Vinci trial management committee
Australian New Zealand Clinical Trials Registry policy advisory committee
Cancer Clinical Trials Development Unit (CTDU) advisory committee, management committee and health economics advisory committee
Cancer Institute NSW board
Cholesterol Treatment Trials’ Collaboration (joint coordinator)
Cochrane Collaboration prospective meta-analysis methods working group
Cooperative Trials Group for Neuro-Oncology (COGNO) scientific advisory committee (deputy chair)
Benefits of Oxygen Saturation Targeting (BOOST II) trial management committee
Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) management committee, executive, and cost-effectiveness subgroup
Intensive Blood Pressure Reduction for Acute Cerebral Haemorrhage Trial (INTERACT) safety and data monitoring committee (chair)
International Breast Cancer Intervention Study (IBIS-II) international steering committee
International Trials of Aspirin to Prevent Recurrent Venous Thrombosis-Embolism (INSPIRE) steering committee (chair)
Long-term Intervention with Piavastatin in Ischaemic Disease (LIPID) management committee, executive, samples subgroup
National Health and Medical Research Council large-scale clinical trials committee (chair)
NHMRC Clinical Trials Centre management review committee and scientific advisory committee
Percutaneous Coronary Angioplasty versus Thrombolysis (PCAT) collaborative group (co-coordinator)
Polypli trial safety and data monitoring committee (chair)
Sentinel Biopsy versus Axillary Clearance (SNAC) trial management committee
Trials associate editor
Virtual Coordinating Centre for International Collaborative Cardiovascular Research (VIGOUR) statistical group (chair) and a VIGOUR leader

Anthony Keech
Asian-Pacific Society of Atherosclerosis and Vascular Disease Prevention executive
<table>
<thead>
<tr>
<th>Committee/Group</th>
<th>Roles/Responsibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia-Pacific Study on CHD Risk Factor Intervention</td>
<td>Management committee (principal investigator and study chairman)</td>
</tr>
<tr>
<td>Cochrane Collaboration</td>
<td>Proactive meta-analysis methods working group (coordinator)</td>
</tr>
<tr>
<td>Early Prevention of Childhood Obesity (EPOC)</td>
<td>Collaboration steering committee, member international clinical trials registry platform</td>
</tr>
<tr>
<td>International Clinical Trials Registry</td>
<td>World Health Organization, best practice group</td>
</tr>
<tr>
<td>International Forum for Standards in Research</td>
<td>Children sample size and data safety monitoring committee subcommittee</td>
</tr>
<tr>
<td>Meta-Analysis of Preterm Patients</td>
<td>Neonatal Oxygen Prospective Meta-analysis (NeOProm) collaboration steering committee</td>
</tr>
<tr>
<td>Perinatal Antepileptic Review of International Studies (PARIS)</td>
<td>collaboration steering committee, writing committee (chair)</td>
</tr>
<tr>
<td>PLOS ONE academic editor</td>
<td>Prevention of Ventilation Induced Lung Injury Collaborative Group (PrevILIG)</td>
</tr>
<tr>
<td>Steering committee</td>
<td>Royal Prince Alfred Hospital clinical trials (ethics) subcommittee</td>
</tr>
<tr>
<td>Amy Boland</td>
<td>Australian and New Zealand Germ Cell Trials Group (ANZ GGTG) operations executive committee</td>
</tr>
<tr>
<td>Australian and New Zealand Urogential and Prostate Cancer Trials Group (ANZUP)</td>
<td>operations executive committee, Accelerated BEP, Aprepitant for Germ Cell Chemotherapy (Sorce and eversun) trial management committees</td>
</tr>
<tr>
<td>Mark Chatfield</td>
<td>Accelerated BEP trial management committee</td>
</tr>
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<td>Aprepitant trial management committee</td>
<td>Aprepitant trial management committee Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP) scientific advisory committee</td>
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<tr>
<td>Chris Brown</td>
<td>Cooperative Trials Group for Neuro-Oncology (COGNO) scientific advisory committee</td>
</tr>
<tr>
<td>Australasian Lung Cancer Trials Group</td>
<td>scientific advisory committee, operational executive committee</td>
</tr>
<tr>
<td>Xanthi Coskinas</td>
<td>Sentinel Node Biopsy versus Axillary Clearance (SNAC) and SNAC 2 trial management committees</td>
</tr>
<tr>
<td>Peta Forder</td>
<td>Australasian Lung Cancer Trials Group scientific advisory committee, operational executive committee</td>
</tr>
<tr>
<td>Cochrane Collaboration</td>
<td>handbook advisory group</td>
</tr>
<tr>
<td>Biostatistics Collaboration of Australia</td>
<td>teaching committee</td>
</tr>
<tr>
<td>Cancer Institute NSW Partnership</td>
<td>operational executive committee</td>
</tr>
<tr>
<td>Laparoscopic Approach to Carcinoma of the Endometrium (LACE)</td>
<td>management committee</td>
</tr>
<tr>
<td>Corona Gainford</td>
<td>Australasian Gastro-Intestinal Trials Group (AGITG) trials operations committee</td>
</tr>
<tr>
<td>Australia New Zealand Gynaecological Oncology Group (ANZGOG)</td>
<td>trials operations committee</td>
</tr>
<tr>
<td>Cancer Institute NSW executive committee, infrastructure grant subcommittee and audit subcommittee</td>
<td>TRIPOD trial management committee (chair)</td>
</tr>
<tr>
<td>Val Gebski</td>
<td>Adjuvant chemotherapy versus surgery alone in patients with stage II AND IIIb gastric adenocarcinoma safety and data monitoring committee</td>
</tr>
</tbody>
</table>
NMRC Singapore Indomethacin study for closure of FDA safety data and monitoring committee
NSW Health Eastern Sydney Area ethics committee clinical trials subcommittee
Oxygen versus air in oxygen-naïve patients with refractory dyspnoea and PaO2<55 safety and data monitoring committee
SNAC trial management committee
Testosterone undecanoate in obese men as adjuvant therapy for a weight loss program safety and data monitoring committee
Trastuzumab with a fluoropyrimidine and cisplatin versus chemotherapy alone as first-line therapy in patients with HER2 positive advanced gastric cancer safety and data monitoring committee
Westmead Cancer Care Joint Radiation Oncology Centre research committee

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Benefits of Oxygen Saturation Targeting (BOOST) II management committee
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Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) management committee
Australian Placental Transfusion Study (APTS) management committee
Australasian Gastro-Intestinal Trials Group (AGITG) trials operations committee
Australia New Zealand Gynaecological Oncology Group (ANZGOG) trials operations committee
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Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) management committee

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Biostatistics Collaboration of Australia writing group

National Curriculum for Entomology evaluation committee
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TRIPOD, Symptom Benefit, PORTEC-3 and Outback trial management committees

Danielle Miller
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Australian and New Zealand Germ Cell Trials Group (ANZ GCTG) operations executive
Australian New Zealand Breast Cancer Trials Group (ANZ BCTG)
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Gynaecological Cancer Intergroup (GCIG) harmonization working group

Rhana Pike
Australasian Medical Writers Association executive committee (vice-president)

Ann Ratcliffe
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Kathleen Scott
NSW Cancer Institute partnership operations executive committee

Co-operative Trials Group for Neuro-Oncology (COGNO) operations executive and scientific advisory committees

Martin Stockler
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Australasian Lung Cancer Trials Group scientific advisory committee
Australia Asia-Pacific Clinical Oncology Research Development (ACORD) workshop steering committee (co-convenor)
Australia New Zealand Gynaecological Oncology Group (ANZGOG) research advisory committee
Australian and New Zealand Breast Cancer Trials Group (ANZ BCTG) scientific advisory committee
Cancer Council Australia national oncology education committee
Cancer Council Australia national oncology education committee
Cancer Trials NSW steering committee, trial selection committee (chair), centre selection committee
Cochrane Collaboration advanced breast cancer working party
Journal of Clinical Oncology editorial board member
National Breast Cancer Centre clinical updates editorial board
National Breast Cancer Centre clinical updates advisory committee
National Breast Cancer Centre hormone therapy working group (chair) and information advisory group (chair)
National Breast Cancer Foundation Strategic research advisory panel
National Cancer Institute (NCI) Intergroup health related quality-of-life committee
NMRC grant review panels for oncology and palliative care strategic grants
University of Sydney Faculty of Medicine oncology block committee (chair), EBM in GMP3/4 (chair), evidence-based medicine resource group, integrated clinical attachment committee and USMP cancer planning committee

Burcu Vachan
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Australian and New Zealand Germ Cell Trials Group (ANZ GCTG) operations executive and executive
Australia New Zealand Gynaecological Oncology Group (ANZGOG) operations executive and research advisory committee
Australasian Lung Cancer Trials Group (ALTG) operations executive and scientific advisory committee

53
Australian New Zealand Breast Cancer Trials Group (ANZ BCTG)
Cancer Institute NSW infrastructure grant subcommittee
Cancer Institute NSW partnership grant operational executive committee

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Sonia Yip
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Australia New Zealand Gynaecological Oncology Group (ANZGOG) operations executive and research advisory committee
Australasian Lung Cancer Trials Group (ALTAG) operations executive and scientific advisory committee
Cooperative Trials Group for Neuro-Oncology (COTGNO) operations executive and scientific advisory committee

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University of Sydney Graduate Medical Program
Cardiology training, Royal Prince Alfred Hospital
Clinical tutor, Royal Prince Alfred Hospital

Lisa Askie
Advanced clinical data management, Master of Health Information Management, University of Sydney
Advanced systematic reviews, Master of Clinical Epidemiology, University of Sydney (co-coordinator)

Controlled clinical trials, Master of Public Health, University of Sydney
Evidence-based medicine in the clinical years, University of Sydney Medical Program

Elizabeth Barnes
Advanced clinical trials, Biostatistics Collaboration of Australia
Basic sciences in oncology, NSW Cancer Council
Controlled clinical trials, Master of Public Health and Master of Medicine, University of Sydney
Principles of statistical inference, Biostatistics Collaboration of Australia

Prunella Blinman
University of Sydney Medical Program

Mark Chatfield
Advanced clinical trials, Biostatistics Collaboration of Australia

Peta Forder
Advanced clinical trials, Biostatistics Collaboration of Australia
Australia & Asia-Pacific Clinical Oncology Research Development (ACORD) workshop faculty
Controlled clinical trials, Master of Public Health and Master of Medicine, University of Sydney

Corona Gainford
University of Sydney Medical Program

Val Gebski
Advanced clinical trials, Biostatistics Collaboration of Australia (coordinator)
Basic sciences in oncology, NSW Cancer Council
Controlled clinical trials, Master of Public Health and Master of Medicine, University of Sydney
Radiation oncology training, RACR trainees, Westmead Hospital, NSW Cancer Council

Adrienne Kirby
Basic sciences in oncology, NSW Cancer Council
Controlled clinical trials, Master of Public Health and Master of Medicine, University of Sydney
Principles of statistical inference, Biostatistics Collaboration of Australia (coordinator)

Sally Lord
Advanced evaluation of diagnostic tests, Master of Public Health and Master of Medicine, University of Sydney

Basic sciences in oncology, NSW Cancer Council
Decision analysis, Master of Public Health and Master of Medicine, University of Sydney
Evidence-based medicine, University of Sydney Medical Program

Andrew Martin
Decision analysis, Master of Public Health and Master of Medicine, University of Sydney
Controlled clinical trials, Master of Public Health and Master of Medicine, University of Sydney

Rebecca Mister
Advanced clinical data management, Master of Health Information and Management, University of Sydney

Rachel O’Connell
Principles of statistical inference, Biostatistics Collaboration of Australia

Lucas Staub
Screening and diagnostic test evaluation, Master of Public Health and Master of Medicine, University of Sydney

Martin Stockler
Australia & Asia-Pacific Clinical Oncology Research Development (ACORD): convenor and chair of international steering committee
Making sense of Cancer Clinical Trials for NSW Medical Oncology Trainees (convener)
Clinical epidemiology for physician trainees, Royal Prince Alfred Hospital
Evidence-based medicine in the clinical years, University of Sydney Medical Program (chair and coordinator)
Medical oncology clinical training, Royal Prince Alfred Hospital
Oncology and palliative care, University of Sydney Medical Program (block chair)
Patient-based measures, Master of Medicine, University of Sydney (course coordinator)
Quality of life in oncology, Cancer Institute NSW

Burcu Vachan
Basic sciences in oncology, NSW Cancer Council
Evidence-based medicine, University of Sydney Medical Program

Diana Zannino
Advanced clinical trials, Biostatistics Collaboration of Australia
Controlled clinical trials, Master of Public Health and Master of Medicine, University of Sydney
Basic sciences in oncology, NSW Cancer Council


Cools F, Henderson-Smart DJ, Offerma M, Askie LM. Elective high frequency oscillatory ventilation versus conventional ventilation for acute pulmonary dysfuction in preterm infants. Cochrane Database of Systematic Reviews 2009; (3): CD001004.


Abstracts


Staub LP, Lord S, Houssami N. Including evidence about the impact of tests on patient management in systematic reviews of diagnostic test accuracy. 17th Cochrane Colloquium; 11–14 October, Singapore. [Thomas C Chalmers MD Award for best poster presentation.]

Staub LP, Lord S, Melloh M, Barz T. Designing clinically relevant test accuracy studies when the perfect reference standard does not exist and binding is not possible. 18th Australasian Epidemiological Association Annual Scientific Meeting; 30 Aug–1 Sep 2009; Dunedin. Received AEA travel award.


Selected invited presentations


Keech AC. Total myocardial infarction, MS profiles: latest results from the FIELD study. European Society of Cardiology Congress; 30 Aug–3 Sep 2008, Munich.


Simes J. Confronting the costs of cancer. The role of clinical trials. Clinical Oncological Society of Australia Annual Scientific Meeting; Nov 2009, Gold Coast.


Stockler M. Prognosticating in advanced cancer. Australia and New Zealand Joint Oncology Scientific Meeting; 6–9 Aug 2008, Christchurch.

Notes