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NHMRC Clinical Trials Centre
The University of Sydney
88 Mallett Street
Camperdown NSW 2500
Australia

(Postal) Locked Bag 77
Camperdown NSW 1450
Australia

Tel: +61 2 9562 5000
Fax: +61 2 9565 1863
Email: enquiry@ctc.usyd.edu.au
Web: www.ctc.usyd.edu.au
The National Health and Medical Research Council Clinical Trials Centre was established in October 1988 by the NHMRC and the University of Sydney. It now has about 100 staff and is a major presence in the world of clinical trials operation and research.

The CTC is a leader in clinical trials research in Australia and is prominent in the South-East Asian and Pacific region. It is a member of worldwide networks of investigators and trial groups, within which it has taken the lead in large-scale multicentre trials and collaborative research projects. An important part of its research program is methodological work in biostatistics. It is an active member of the global Cochrane Collaboration, which seeks and assesses research evidence for health care. The CTC also offers consulting services in the area of trials and trials methodology and training placements for postgraduate students.

This report covers the calendar year 2003. It aims to present the activities and achievements of the CTC over the year, relating these to its plans for 2004.
DIRECTORS OF THE CTC

John Simes is the foundation director of the CTC and continues to direct all the CTC's activities. He is recognised internationally for his expertise in the field of clinical trials and represents the CTC on many national and international committees. He is also professor in the departments of Medicine and Public Health and Community Medicine at the University of Sydney, and specialist medical oncologist at Royal Prince Alfred Hospital. He holds an MD from the University of Sydney in the area of cancer trials and an MSc from Harvard in biostatistics.

Tony Keech, cardiologist and epidemiologist, is deputy director of the CTC, which he joined in 1992 after more than five years at Clinical Trials Research Unit of Oxford University in the UK. He is an associate professor in the Department of Medicine at the University of Sydney and a practising consultant cardiologist at Royal Prince Alfred Hospital. He is a member of many national and international committees, including multinational trial steering committees.

Professor Keech is chairman of the FIELD study on heart disease and diabetes, the largest trial involving diabetic patients, and he has a special interest in heart disease in the Asian-Pacific area.
**Dorothea Sophia** is business director of the CTC, with responsibility for finance, human resources, information technology services and general administration. She has been with the University of Sydney since 1989, first as resources manager to the Faculty of Science and then as college administration manager (resources) to the College of Sciences and Technology (faculties of Agriculture, Architecture, Engineering, Science and Veterinary Science and Orange Agricultural College).

Before joining the university, she worked for various media organisations, including the Fairfax Group, SBS Television and ABC Radio.

**Wendy Hague** is clinical trials programme director of the CTC, and is primarily responsible for the successful conduct of the CTC’s large-scale, multicentre clinical trials and ensuring that trials systems, procedures and methods are of the highest standard. She was active in obtaining the trials infrastructure grant, and is overseeing the development of the new generic web-based data management system.

Wendy has medical qualifications and an MBA. She came to the CTC in 1990, as manager of the LIPID trial, after seven years’ experience working in clinical trials in the pharmaceutical industry.
2003 was the first year of funding from our new NHMRC five-year program grant. This has allowed us to continue, and extend, our concentration on research that is important to public health. Our research program consists of initiating major new trials where these are needed; combining evidence from trials and integrating the evidence with patients’ individual risks and preferences; and improving methods of biostatistical analysis and health outcome assessment.

New trials

A health risk affecting many people is venous thrombosis. Each year over 20 000 Australians develop blood clots with no underlying cause. In 2003, we began ASPIRE, the first trial of using aspirin after routine warfarin therapy to prevent recurrent thrombosis in people at risk. Aspirin is a cheap and widely available treatment, and part of the research will be to investigate any national cost savings of using this treatment. From 2004, the trial will be partly supported by an NHMRC project grant.

INIS is a trial of immunoglobulin therapy for newborn babies with severe infections. In Australia and New Zealand about 2500 babies are born with infections that put them in danger of death or disability. The CTC is coordinating the Australian and New Zealand part of this large international trial. In 2003 the CTC was awarded a project grant from the NHMRC which, together with other funding, will secure the future of this important trial.

Cancer

Cancer trials research is usually undertaken by national and international collaborative groups of clinical specialists, trial coordinators and statisticians. The CTC is proud to be part of several of these collaborations, whose achievements were substantial in 2003. Our trials cover the range of gastrointestinal cancer, breast cancer, and gynaecological cancer, as well as trials and research applicable to cancer patients in general.

The CTC is the trials coordinating centre and secretariat for the Australasian Gastro-Intestinal Trials Group. The group works with other cancer investigators worldwide and takes part in international projects. In 2003 AGITG launched two new studies. One is VICTOR, a large international trial of rofecoxib for colorectal cancer, which is ready to begin randomisation early in 2004. The other, CO17, is investigating the effect of treatment with a monoclonal antibody, cetuximab, on the survival of patients with colorectal cancer. This trial has randomised its first Australian patient.

A major recently initiated trial has been SNAC, which is comparing two ways of detecting whether cancer cells have spread from the breast into the lymph nodes of women with early breast cancer. The current standard method is removing all the axillary lymph nodes, damaging the lymph system and leaving the women at risk of serious long-term arm swelling and pain. In the newer method, only the first lymph nodes are removed routinely. Since mid-2002, recruitment to this trial has been exceptionally rapid. The trial should be completed well ahead of its target date. The results will tell whether the new less intrusive diagnostic method is safe and effective.

Taxanes, such as paclitaxel and docetaxel, are the most active chemotherapy agents in the management of advanced breast cancer. The Cochrane Collaboration’s breast cancer group, which is based at the CTC, completed a major review for the international Cochrane Library of the evidence for using taxane-containing regimens; they appear to improve overall survival, time to progression and overall response in women with metastatic breast cancer.
Cardiovascular trials

The CTC’s **FIELD trial** is the largest trial ever conducted in Australia. During 2003, FIELD’s investigators have monitored the health and wellbeing of over 9000 people with diabetes from Australia, New Zealand and Finland. In recent years, adult diabetes has been recognised as a widespread and growing major health issue. The trial is on track to be completed early in 2005. By then each patient will have been followed up for between 4 and 7 years. A trial of this size provides enough data for additional research questions and substudies of particular patient groups. Several of these were planned as part of the trial protocol and others are emerging with time.

An earlier large-scale trial, **LIPID**, was completed in 1998, but the CTC is continuing to follow up the patients and record new data on the long-term effects of cholesterol-lowering therapy. LIPID is a rich data source for gaining insights and new knowledge into cardiovascular disease. In 2003 papers reporting on the benefits of treatment for the women in LIPID and the subgroup of patients with diabetes were published. The data are also being used for further analyses of cost-effectiveness and quality of life.

Reviews of new procedures

Government health policy should rely on well-founded evidence. As a service to government, staff at the CTC, in association with subject specialists, compile and assess the evidence for the worth of **new clinical procedures** in relation to existing remedies. In 2003, our reports included studies of gastric banding for morbid obesity and radiation therapy for liver metastases from colorectal cancer.

Methodological research

**CTC biostatisticians**, with expertise in study design, have a central role in the trials coordinated by the CTC and as members of collaborative groups. As external consultants, they also guide other groups in design and conduct of their trials and analysis of their data. Several such partnerships have been continuing through 2003. Other CTC achievements include:

- **The Clinical Trials Data and Information Network project** (now called **Flexetrials**) was begun in 2002 and is now more than half-way through its development. It is a generic system for web-based trials, which will be used by the CTC and others to conduct trials in areas of need and to train people in the conduct of trials. Its development over three years has been funded by the Department of Education, Science and Training.

- Researchers from the CTC have been instigators and authors of the series in the Medical Journal of Australia, *Trials on trial*: the essentials of clinical trials in 22 short articles. The series is an attempt to confront the problem of poorly conducted trials and inadequate reporting of trials. We are two-thirds of the way through the series, which is due to be complete in 2004.

Our research team, systems developers, clinical trial staff and support staff have created an ideal base on which to advance and integrate trial methods and research. We have been working effectively with national and international clinical investigators and have ongoing commitments from them. The CTC is well-placed to meet its aims of bringing about more reliable and more valid trial results, more effective use of trial evidence in clinical decision making, and ultimately better health outcomes.

The directors
BUSINESS MANAGEMENT

Business management in the CTC uses its vision, mission and values as a basis for its processes.

Vision: To be the leader of clinical trials research excellence, the benchmark for the conduct of investigator-initiated clinical trials and the preferred reference for translating clinical trials evidence into practice.

Mission: To achieve best practice in health care and to improve outcomes in Australia and internationally through the use of clinical trials.

Values: The CTC is committed to excellence in its contribution to evidence-based health care in public and community health and to rigour in the acquisition, creation, analysis, interpretation, synthesis, translation and transmission of knowledge.

In human resources, during the past year the CTC placed its commitment to staff as a priority and embarked on clinical trials recruiting in response to continued growth in clinical trials research, as well as executive recruiting to enable us to put into practice the matrix management model. This matrix supports flexibility in leadership, provides consistency across projects and resources and reinforces the collective use of competencies for strategic management of clinical trials and other related projects.

We remain committed to implementing a learning culture as part of our work practices and this year, to support our leaders, the 2003 CTC leadership program focused on two important aspects of leadership and management capability: understanding emotional intelligence and its role in leadership behaviour, and the leader as coach interactive workshops.

The CTC introduced a new category of staff—clinical trials assistants—as a gateway for interested people who are willing to use their studies or experience to pursue a career in clinical trials by undertaking a range of support roles for research teams.
### FUNDING IN 2003

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<tr>
<th>Granting body and project</th>
<th>Centre</th>
<th>Regional</th>
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## Granting body and project

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<th>Centre</th>
<th>Regional</th>
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<td><strong>TOTAL FUNDING</strong></td>
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CLINICAL TRIALS
2003 has been a year of consolidation with respect to clinical trials, with considerable review and streamlining of many processes and procedures—in the oncology group in particular. Several trials were initiated or started operation. In oncology, CO17 began late in 2003. The ASPIRE pilot study commenced recruitment in May 2003 and was awarded partial funding by the NHMRC in November this year. The INIS trial is in its second year of recruitment and is progressing extremely well: 293 patients from Australia and New Zealand had been randomised by the end of December 2003.

The new tripartite management structure for the oncology group was bedded down this year. Haryana Dhillon is responsible for trials development, and Burcu Cakir and Sonia Yip are managing trials operations, under the direction of the trials program manager.

The implementation of the matrix model for trials management was realised in three new positions—head of site management, currently held by Kathleen Scott, head of randomisation, held by Andrew O’Callaghan (both new CTC appointments), and head of data management, accepted by Susan Wonders, the CTC’s most experienced data manager.

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The head of site management ensures that qualified sites are selected, that ethics and regulatory approvals are properly obtained in order for sites to be initiated, that reporting is according to protocol, and that closure of sites and the reporting of data are timely. In the CTC, data management has always been at the forefront of our activities. The head of data management ensures compliance with regulations across the trials of the CTC.

These new positions have defined and clarified procedures in their domains. They support the trial coordinators in planning and implementing these aspects of their projects. In addition, the CTC has used the services of two consultants to guide the implementation of project management principles and software for our trial coordinators. All the CTC’s clinical trials are now planned and tracked using a template developed in MS Project.

Major work continued in 2003 on the specifications for the development of generic web-based data systems for clinical trials conduct and management to improve project set-up, conduct and close-down times (the CTDIN project).

With the help of the CTC’s external quality-assurance consultant, Philippa Smith, work has continued on developing and refining the standard operating procedures. Gemma Ritchie, the quality-assurance manager, launched a major staff training activity with the support and assistance of Philippa and other senior trials staff.
The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) trial was a multicentre trial begun in 1990, studying the effects of pravastatin in 9014 patients with coronary heart disease and average cholesterol levels.

The randomised phase of the trial finished in 1997 and showed that pravastatin significantly reduced the risk of death, myocardial infarction and other cardiovascular events. At this time, further consent was obtained from 7680 patients completing the main trial to continue with long term follow-up until at least 2003. For the first two years (1997–1999), patients continued to be followed up through local study clinics, and were offered pravastatin therapy. Results from this phase showed that pravastatin therapy during the randomised phase of the study continued to have a beneficial effect.

After 1999, funding for clinic visits ceased and patients have since been followed centrally from the CTC, which has coordinated the study since its inception. The aim of the extended follow-up is to examine the long-term safety and cost-effectiveness of pravastatin treatment over at least 10 years, and to assess the effects of treatment on outcomes such as total mortality, coronary heart disease mortality, acute myocardial infarction, stroke, cancer and other major cardiovascular events. Approval for the study to continue long-term follow-up has been granted by the Human Ethics Committees of the 86 study sites in Australia and New Zealand, and the University of Sydney Human Ethics Committee.

During 2003, the remaining cohort of 6663 patients was followed up by two methods. First, all were sent a reply-paid questionnaire. Included with this was a newsletter updating participants with continuing results from the LIPID study plus other health-related information. Nonresponders received a reminder letter then a follow-up phone call. Other methods of patient searching used included internet directories and electoral rolls.

Second, national and state registers of mortality and morbidity information were accessed. Data were matched with the New Zealand Health Information Service data set, the Australian Institute of Health and Welfare national death index and the Health Department of Western Australia hospital morbidity, mortality and cancer registry data set. Ethics approvals are being sought for further data matching with the National Cancer Statistics Clearing House at the Australian Institute of Health and Welfare.

Blood samples collected during the earlier phase of the study are being analysed in relation to various risk factors and biomarkers for cardiovascular disease.

Papers on the effects of pravastatin in women and in diabetic patients were published in 2003.
FIELD TRIAL

FIELD - Fenofibrate Intervention and Event Lowering in Diabetes started in February 1998 in Australia, New Zealand and Finland. The full enrolment of 9795 participants was achieved in November 2000. The study sponsor is Fournier Pharma of France.

The study aims to determine whether treatment with fenofibrate (a Fournier Pharma product), a potent modifier of blood lipid levels, will reduce the risk of fatal coronary heart disease in people with type 2 diabetes.

Fenofibrate acts to raise blood levels of high-density lipoprotein cholesterol (HDL, the protective cholesterol form) and reduce low-density lipoprotein cholesterol (LDL) and triglyceride levels.

FIELD will determine whether strokes and deaths can be prevented in people with diabetes treated with fenofibrate.

The study participants will continue to have 6-monthly visits until December 2004, and then all participants will attend for a final visit in the first quarter of 2005.

It is planned that the results of the study will be available in November 2005.

The FIELD team, from left: Bei Zhong, Jianpeng Gu, Li Ping Li, Samir Doshi, Sarah Blakesmith (seated), Tatiana Sourjina, Colin Sutton, Sharon Walder, Kew Flood, Libby Keirnan, Tony Keech (seated), Ainesh Pillai, Sonia Gillies, Diane Schipp, Peta Forder (seated), Zaved Hossain, Russell Taylor, San Chan, Faith Papuni
The scientific meeting of Australian and New Zealand FIELD investigators was held at the Gold Coast, Queensland, in July 2003. It was attended by the CTC FIELD team, study coordinators and investigators from Australian and New Zealand sites, representatives of the sponsor, Fournier Pharma. Progress reports on various aspects of FIELD were presented as part of a program of current diabetes research.

Guest speaker, Bob Gibson, professor, Flinders Medical Centre and the Women's and Children's Hospital, Adelaide, spoke on omega-3 fats in the diet. Another highlight was the debate on the place of glycaemic index in monitoring diabetic diets, with debaters, Jennie Brand-Miller, professor, School of Molecular Biosciences, University of Sydney, and John Munro, research leader, nutrition and health team, New Zealand Institute for Crop and Food Research.

Main eligibility criteria

- type 2 diabetes mellitus with onset after the age of 35 years
- men and women aged 50–75 years of age
- average total cholesterol 3.0–6.5 mmol/L
- triglycerides/high-density cholesterol ratio of \( \geq 4.0 \), or triglycerides \( >1.0 \) mmol/L

It is projected that about 500 coronary heart disease events will have occurred by February 2005, by which time the trial will have 80% power to detect a 25% reduction in CHD events (assuming that all patients continue to take the allocated drug) or a 20% reduction in CHD events (based on the intention-to-treat analysis); this will also provide more than 90% power to detect a 30% relative reduction in CHD events (25% on the basis of the intention-to-treat analysis).

The CTC FIELD team has 22 members. There were some changes in 2003. Joining the team in Australia were Sharon Walder and Stefan Czyzewski as clinical trial associates, Samir Doshi as finance manager, Karen Pinto as documentation and compliance coordinator and Diane Schipp as serious adverse events coder. Sarah Blakesmith was promoted to clinical trial coordinator, Claudia Anderson to data manager, special projects, and Kew Flood and Sonia Gillies to clinical trial assistant.

During 2003, systems and quality assurance work was steered by the FIELD information systems team: Bei Zhong and Jianpeng Gu with manager, Colin Sutton. Bei and Jianpeng have worked on the FIELD database since its inception. Their work in 2003 will be instrumental to the delivery of the study results in 2005.

The FIELD New Zealand and Finnish project offices continue to be ably coordinated by Dr Caroline Lintott in Christchurch and Anne Salo in Helsinki.

FIELD investigators stay up to date

The scientific meeting of Australian and New Zealand FIELD investigators was held at the Gold Coast, Queensland, in July 2003. It was attended by the CTC FIELD team, study coordinators and investigators from Australian and New Zealand sites, representatives of the sponsor, Fournier Pharma. Progress reports on various aspects of FIELD were presented as part of a program of current diabetes research.

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The International Neonatal Immunotherapy Study (INIS) is a major international, double-blind, placebo-controlled randomised trial of immunoglobulin for newborn babies with serious infection that puts them at risk of death or permanent disability.

Newborn infants, particularly those born early, are deficient in immunoglobulin (IgG) and so are at risk of infection. Each year over 2500 babies in Australia and New Zealand develop serious infection: about 250 die and another 375 survive with lifelong disability. Polyclonal intravenous immunoglobulin (IVIG) may help to reduce death and brain inflammation resulting from infection.

The CTC is the coordinating centre for Australia and New Zealand and is making particular contributions to the trial by:

• assessing its economic implications by undertaking an economic evaluation
• reporting informative and unique clinical data on the type, frequency and outcomes of serious infections specific to neonatal units in Australia and New Zealand
• validating the follow-up questionnaires for parents in a local setting
• examining whether IVIG results in subtle cognitive differences between the two groups.

Eligibility criteria

• a proven or suspected serious infection, and
• a birth weight under 1500 grams, or receiving artificial respiratory support by endotracheal tube, or having evidence of infection in a normally sterile site, and
• antibiotics already prescribed

Study drug

Intragam® P, 500 mg (8.3 ml) per kg or normal saline placebo given over 4 to 6 hours and repeated after 48 hours

Planned recruitment: 5000 infants internationally, 1500 in Australia and New Zealand

Recruitment in 2003: 464 internationally, 206 in Australia and New Zealand

Outcome measures

Primary

• survival free of major disability at two years, corrected for gestational age

Secondary

• chronic lung disease or major cerebral abnormality before hospital discharge
• positive culture after trial entry
• necrotising enterocolitis
• pneumonia
• duration of respiratory support
• nonmajor disability
• length of hospital stay
• number of hospital admissions

Funding: Sydney University Sesqui grant, Telstra Foundation, Ian Potter travel grant, NHMRC, Financial Markets Foundation for Children, NZ Health Research Council, UK Medical Research Council.

By the end of 2003, there were 15 participating hospitals in Australia and New Zealand; another 10 were due to start by early 2004.
**ASPIRE TRIAL**

Aspirin to prevent recurrent venous thromboembolism (ASPIRE) is a multicentre, randomised double-blind placebo-controlled clinical trial examining the efficacy and safety of low-dose aspirin after initial oral anticoagulation to prevent recurrent venous thromboembolism.

Each year, an estimated 20,000 Australians develop a new episode of deep-vein thrombosis or pulmonary embolism, of which one-third are unexplained. As many as 5000 each year have another episode, and several hundred die of fatal pulmonary embolism. This trial meets the need to identify a simple, safe, effective and widely applicable strategy for preventing recurrence of venous thromboembolism.

**Eligibility**

A first episode of unprovoked proximal deep-vein thrombosis or pulmonary embolism that has been treated with heparin and warfarin.

**Study drug**

- acetylsalicylic acid (aspirin)

**Main outcome measures**

**Primary**

- symptomatic venous thromboembolism or fatal pulmonary embolism

**Secondary**

- total vascular events (cardiovascular death, symptomatic venous thromboembolism, myocardial infarction or stroke)
- net clinical benefit (death, major vascular event or major bleed)

**Planned recruitment:** 3000 patients to be recruited over 3 years

**Funding:** NHMRC, Bayer, Australasian Society of Thrombosis and Haemostasis

In 2003, the pilot phase of the study commenced and in the second half of the year 23 patients were randomised at 3 sites.

The pilot phase, with about 100 patients, will continue until mid-2004, when the main study is expected to begin.
The oncology program at the CTC has undergone structural changes leading to growth of this discipline. The number of staff increased from 8 to 18 in 2003 (this included managerial, trial coordinator, data manager, and the new clinical trial assistant positions). The emergence of oncology development and operational trials programs (in addition to the patient preferences, quality-of-life and cost-effectiveness sectors) has enabled streamlined procedures for advancing new trial protocols and implementing existing trial operations.

The oncology program maintained close associations with national and international collaborative groups, this year including the National Cancer Institute in Canada (the AGITG CO17 trial).

The CTC is secretariat and coordinating centre for the Australasian Gastro-Intestinal Trials Group (AGITG), the NSW Cooperative Oncology Group (NCOG) and the ANZ Germ Cell Tumour Study Group and the Australia–New Zealand Gynaecological Oncology Group (GOG).

Organisational structure of the CTC oncology group
Breast cancer trials

Sentinel node biopsy versus axillary clearance: the SNAC trial

Cooperative group: Royal Australasian College of Surgeons (RACS)

Participants
Women with operable breast cancer in whom lymph-node staging is indicated

Outcome measures
- early axillary morbidity
- lymphoedema
- axillary tumour recurrence
- survival
- disease-free survival
- use of adjuvant therapies
- number of surgical episodes
- days in hospital

Recruitment: 831 patients from 32 centres

Recruitment target: 1000


The SNAC trial is the first large trial of surgical treatment of breast cancer in Australasia. It is expected to provide important information on the effects of axillary surgery and the quality of life of women having breast cancer surgery.

When data from this trial are combined with data from other similar international trials, a meta-analysis will have adequate power to show whether axillary surgery influences recurrence of breast cancer and survival.

A preliminary analysis of data from the first 150 patients is being undertaken.

An investigators’ meeting was held for SNAC during the annual meeting of the Royal Australasian College of Surgeons in Brisbane, May 2003. A training day for data managers and research nurses was held at the CTC in November 2003.

Xanthi Coskinsas, SNAC trial coordinator

Recruitment to the SNAC trial over the first 2 years of the trial
The CTC is the randomisation and statistical centre for the **Australian and New Zealand Breast Cancer Trials Group (ANZ BCTG)**, which is an integral part of the International Breast Cancer Study Group (IBCSG). The CTC has also been involved in quality-of-life and cost-effectiveness studies for this group.

**Active trials of the Australian and New Zealand Breast Cancer Trials Group**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants</th>
<th>Outcome measures</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBIS: International breast intervention study</td>
<td>Double-blind placebo controlled randomised trial of tamoxifen (20 mg/day) for 5 years in women aged 35-70 who were at increased risk of breast cancer</td>
<td>• incidence of breast cancer (including ductal carcinoma in situ) • toxicity</td>
<td>Accrual was completed in March 2001. The CTC and ANZ BCTG are leading a quality-of-life and cost-effectiveness sub-study. Data are being collected at baseline and at regular intervals during follow-up. The follow-on IBIS II trial is expected to start randomising patients in 2004.</td>
</tr>
<tr>
<td>ATLAS: Adjuvant tamoxifen: longer against shorter</td>
<td>Patients with previous breast cancer, clinically free of cancer, on tamoxifen therapy, and uncertain whether to stop</td>
<td>• all-cause mortality • cause-specific mortality • nonfatal events (including new, contralateral breast cancer, myocardial infarction and other vascular events requiring hospitalisation)</td>
<td>Target recruitment: 20 000 international, 1200 Australia and New Zealand Recruitment to 2003: 629</td>
</tr>
<tr>
<td>IBCSG 16-98, BIG 2-97: Exemestane vs tamoxifen as adjuvant therapy for postmenopausal women with primary breast cancer who have received adjuvant tamoxifen for 2-3 years</td>
<td>Postmenopausal women after breast cancer, without recurrence, who are currently receiving tamoxifen</td>
<td>• disease-free survival • overall survival • incidence of contralateral breast cancer • long-term tolerability of the regimens</td>
<td>Recruitment target: 2200 Recruitment to 2003: 70</td>
</tr>
<tr>
<td>HABITS: Randomised trial of HRT after previous radical breast cancer treatment (IBCSG 17-98, BIG 3-97)</td>
<td>Perimenopausal and postmenopausal women with previously treated breast cancer and no evidence of recurrence</td>
<td>• relapse-free survival • quality of life</td>
<td>International recruitment target: 1300 Recruitment to 2003: 14</td>
</tr>
<tr>
<td>IBCSG 18: Evaluation of letrozole as adjuvant endocrine therapy for postmenopausal women with receptor-positive tumours</td>
<td>Postmenopausal women after surgery, with oestrogen-positive or progesterone-positive tumours</td>
<td>• overall survival • disease-free and systemic disease-free survival • safety and tolerability of the study drugs</td>
<td>International recruitment target: 6100 Recruitment to 2003: 667</td>
</tr>
<tr>
<td>Trial</td>
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<td>Outcome measures</td>
<td>Status</td>
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</table>
| ANZ 0001: Phase III trial of oral chemotherapy with capecitabine versus standard chemotherapy with CMF for advanced breast cancer | Women with advanced breast cancer and no prior chemotherapy for advanced disease                                                                 | • tumour response  
• survival  
• quality of life | Recruitment target: 465  
Recruitment to 2003: 213 |
| IBCSG 22: Low-dose cytotoxics as antiangiogenesis treatment after adjuvant induction chemotherapy for patients with oestrogen-negative or progesterone-negative breast cancer | Women with oestrogen-negative or progesterone-negative breast cancer who have had surgery, including axillary dissection | • efficacy                                                                                             | Recruitment to 2003: 1                      |
| ANZ 0102, BCIRG 007: Taxotere and herceptin vs taxotere, carboplatin and herceptin as first-line chemotherapy for patients with advanced breast cancer | Women with advanced breast cancer, with no previous chemotherapy for advanced disease, and HER2 gene amplification and normal cardiac function | • disease-free survival  
• overall survival  
• toxicity | International recruitment target: 444  
Recruitment to 2003: 18 |
| ANZ 0201: Iressa (gefitinib) in patients with hormone insensitive or hormone-resistant metastatic or inoperable locally advanced breast cancer | Women aged 18 years and over with metastatic or inoperable locally advanced breast cancer, either:  
• hormone-receptor negative (oestrogen and progesterone)  
• hormone-receptor positive (oestrogen or progesterone) with disease progressing after 2 previous hormone treatments (tamoxifen and aromatase inhibitor) | • tumour response  
• overall survival  
• progression-free survival | Recruitment target: 90  
Recruitment to 2003: 56 |
Australasian Gastro-Intestinal Trials Group (AGITG)

The CTC is the trials coordinating centre and secretariat for the Australasian Gastro-Intestinal Cancer Trials Group (AGITG). This includes collaboration with the National Surgical Adjuvant Breast and Bowel Project (NSABP), the European Organisation for Research and Treatment of Cancer (EORTC), the Eastern Cooperative Oncology Group (ECOG) and the Singapore Clinical Trials Research and Epidemiology Unit.

Recruitment for the C-07 trial of colon cancer was completed in 2003. The main results of the advanced hepatocellular carcinoma trial were presented by Jonathan Cebon at the American Society of Clinical Oncology in May. The results of the oesophageal cancer trial (IG9401) have been submitted for publication.

Trials of the Australasian Gastro-Intestinal Trials Group

<table>
<thead>
<tr>
<th>Trial</th>
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<th>Main outcome measures</th>
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</tr>
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<tbody>
<tr>
<td>Pilot phase II study of Sandostatin LAR in patients with advanced hepatocellular carcinoma</td>
<td>Patients with advanced resectable hepatocellular carcinoma.</td>
<td>• feasibility and safety of treatment&lt;br&gt;• effects of somatostatin receptor levels on outcomes</td>
<td>AGITG recruitment: 63&lt;br&gt;Recruitment target: 60</td>
</tr>
<tr>
<td>EORTC 40983: Preoperative and postoperative chemotherapy with oxaliplatin, 5-fluorouracil and leucovorin versus surgery alone in resectable liver metastases of colorectal origin</td>
<td>Patients with potentially resectable liver metastases of colorectal origin and no prior therapy for advanced disease.</td>
<td>• progression-free survival&lt;br&gt;• survival</td>
<td>AGITG recruitment: 32&lt;br&gt;Recruitment target: 40&lt;br&gt;International recruitment: 321</td>
</tr>
<tr>
<td>Clinical activity of STI-571 at 2 dose levels in patients with unresectable or metastatic gastrointestinal stromal tumours (GIST) expressing the KIT receptor, tyrosine kinase (CD117)</td>
<td>Patients with a histologically documented diagnosis of unresectable or metastatic GIST, incurable with any conventional multi-modality approach.</td>
<td>• progression-free survival&lt;br&gt;• survival&lt;br&gt;• tumour response</td>
<td>AGITG recruitment: 116&lt;br&gt;International recruitment: 845&lt;br&gt;Target: 600</td>
</tr>
<tr>
<td>C-06: Oral uracil/ftorfur plus leucovorin compared with 5-fluorouracil plus leucovorin in the treatment of patients with stages II and III carcinoma of the colon</td>
<td>Patients with stages II and III adenocarcinoma of the colon, no metastatic disease and a life expectancy of at least 10 years (excluding diagnosis of cancer)</td>
<td>• disease-free survival&lt;br&gt;• survival&lt;br&gt;• quality of life&lt;br&gt;• prognostic significance of genetic and biologic markers</td>
<td>AGITG recruitment: 11&lt;br&gt;International recruitment: 1642&lt;br&gt;Target: 1500</td>
</tr>
</tbody>
</table>
## Trial Participants Main outcome measures Status

<table>
<thead>
<tr>
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</table>
| C-07: 5-fluorouracil plus leucovorin and oxaliplatin compared with 5-fluorouracil plus leucovorin for patients with stages II and III carcinoma of the colon | Patients with stages II and III adenocarcinoma of the colon, no metastatic disease and a life expectancy of at least 10 years (excluding diagnosis of cancer) | • survival  
• disease-free survival | AGITG recruitment: 134  
International recruitment: 2492  
Target: 2472 |
| IG9401: Surgery alone compared with concurrent preoperative chemotherapy and radiation and by surgery for localised resectable carcinoma of the oesophagus | Patients with operable cancer of the oesophagus | • progression-free survival  
• overall survival  
• treatment toxicity  
• quality of life | AGITG, TROG recruitment: 257 patients  
Recruitment target: 250 |
| CO17: Cetuximab and best supportive care compared with best supportive care alone in treating patients with metastatic epidermal growth factor receptor-positive colorectal cancer | Patients with progressing metastatic colorectal cancer that is positive on testing for epidermal growth-factor receptors | • progression-free survival  
• overall-survival  
• treatment toxicity | AGITG recruitment: 1  
AGITG recruitment target: 100  
International recruitment target: 500 |
| VICTOR: Phase III, double-blind, placebo-controlled study of rofecoxib (Vioxx) in colorectal cancer patients, following potentially curative therapy | Patients with Dukes stage II or stage III colorectal carcinoma and no evidence of residual disease after surgery | • progression-free survival  
• overall-survival  
• treatment toxicity | AGITG recruitment target: 1000  
International recruitment target: 7000 |
The Australia New Zealand Gynaecological Oncology Group (ANZGOG) works to improve outcomes for women with gynaecological cancer via a coordinated approach to clinical trials research. The group is a member of the international Gynecological Cancer Intergroup (GCIG) and the United States Gynecological Oncology Group (US GOG), and is also linked with the Australian Ovarian Cancer Study, a large translational and epidemiological study funded by the US National Cancer Institute (NCI).

Recruitment to the ANZGOG 0201 trial has been extremely rapid. The first interim analysis is due in the first quarter of 2004.

The GOG 182 trial is in the recruitment phase. The GOG 191 trial was suspended to recruitment in September 2003 owing to a higher than expected incidence of thromboembolic events with erythropoietin.

<table>
<thead>
<tr>
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</table>
| ANZGOG 0201: Phase II trial of weekly docetaxel (Taxotere) for patients with relapsed ovarian cancer who previously received paclitaxel | Women with epithelial ovarian cancer, fallopian tube cancer or peritoneal cancer who previously received paclitaxel and have an elevated serum CA-125 or measurable disease | • response  
• toxicity                     | Recruitment: 11  
Target: 60                                                |
| GOG 182: Phase III randomised trial of paclitaxel and carboplatin versus triplet or sequential doublet combinations in patients with epithelial ovarian or primary peritoneal carcinoma | Women with advanced (stage III or IV) primary ovarian or peritoneal cancer | • survival  
• toxicity  
• disease-free survival                  | International recruitment target: 3000-4000  
Target, Australia and New Zealand: 400                          |
Advanced cancer

ZEST: Zoloft's effects on symptoms and survival time in advanced cancer
Investigator-initiated trial: NSW Cooperative Oncology Group, NSW Cancer Council, SA Cancer Council

Participants
People with advanced cancer in whom there is doubt about the benefits of treatment with antidepressants.

Outcome measures
• quality of life (depression, anxiety and fatigue)
• survival

Recruitment: 71 (target 440)

Funding: NSW Cancer Council, Pfizer Australia, Pfizer International and Cancer Trials NSW

Antidepressant drugs increase wellbeing in people with advanced cancer. They may also reduce fatigue and improve overall quality of life.

The ZEST trial will ascertain whether sertraline, an antidepressant, improves subjective wellbeing and survival in a broad cross-section of people with advanced cancer who feel depressed, tired or weak, but do not have major depression.

At the scientific meeting of the Clinical Oncological Society of Australia’s in 2003 in Perth, WA, the ZEST trial was used to illustrate the process of obtaining informed consent in placebo-controlled trials. This workshop was led by Professor Phyllis Butow and Dr Fran Boyle and used an actor from the Pam MacLean Communication Centre. Data managers and research nurses from Australia and New Zealand were taught skills on how to better communicate with potential trial participants.

Patients with advanced cancers

- sertraline 50 mg daily
- placebo daily

Depression, survival, quality of life, adverse events, costs

Julie Poulter and Sarah Krapf
Other cancer trials

Inpatient and outpatient chemotherapy compared
Investigator-initiated trial: NSW Cooperative Oncology Group

Participants
Patients commencing a chemotherapy regimen including at least two cycles of treatment with 100 mg or more of cisplatin, administered as a single dose.

Outcome measures
- patient preference
- cost-effectiveness
- quality of life

Recruitment: 63
Funding: NSW Cancer Council program grant

The primary objective of this randomised unblinded crossover trial is to assess whether patients prefer to have high-dose cisplatin as a hospital inpatient or outpatient (patients are randomised to receive either first and then cross over to the other arm; a minimum of two cycles of cisplatin is required). Secondary objectives are to assess directly differences between outpatient and inpatient administration in direct costs, quality of life, the incidence of adverse events, and the ability to deliver full doses of chemotherapy in subsequent cycles.

Recruitment was complete early 2003. Statistical analyses are under way.

QUART: Patient preferences, quality of life and adjuvant radiation therapy for women with early breast cancer
NHMRC CTC and Department of Public Health and Community Medicine, University of Sydney

Participants
Women having adjuvant radiotherapy for early breast cancer

Outcome measures
- quality of life during and after radiation therapy
- preferences for adjuvant radiotherapy

Complete recruitment: 161
Funding: University of Sydney Cancer Research Fund

Quality of life data have been collected and will be reported in the second quarter of 2004. Preference interviews are being done and will be reported in the last quarter of 2004.
RESEARCH AND SERVICES
SYSTEMATIC REVIEW and META-ANALYSIS

Systematic reviews

Our focus is to provide independent, transparent and scientifically rigorous reviews of health care evidence. Systematic reviews of the evidence are essential to developing and implementing best-practice guidelines.

Systematic reviews are a powerful tool for answering important clinical questions when a single definitive large-scale trial has not been conducted. They combine the results of all relevant high-quality studies that address the same clinical question.

A properly conducted systematic review:

- defines the elements of the research question (the patient population, the intervention being evaluated, the intervention it is to be compared with, and the outcomes)
- defines the methods to be used before the review commences
- documents them in a review protocol.

A comprehensive search strategy is developed to identify studies within the scope of the review. All eligible studies are critically appraised and summarised. Statistical methods for combining the study results (meta-analysis) are used when appropriate.

Reviews of technologies and procedures

Health technology assessment, using systematic reviews, is an important component of evidence-based health policy. The reviews evaluate new technologies and procedures with regard to their safety, effectiveness and cost-effectiveness. The evaluation of a diagnostic test includes an assessment of its accuracy, therapeutic impact and effect on health outcomes.

The CTC advises the Department of Health and Ageing on methods for critically evaluating evidence about new technologies. In collaboration with expert advisers, it also undertakes formal reviews for the department’s Medical Services Advisory Committee (MSAC), which uses the information in making decisions about funding new (and sometimes existing) procedures. These reviews are published on the department’s website at http://www.health.gov.au/msac.

Cochrane Collaboration

Since 1998, the CTC has been home of the Cochrane Breast Cancer Group (CBCG) and the Cochrane Prospective Meta-Analysis Methods Group. The Cochrane Collaboration is an international group of health care providers, researchers, consumers and policy makers who are committed to ensuring that decisions made concerning all aspects of health care are based on sound evidence.

The processes involved in preparing and maintaining Cochrane reviews...
Currently there are 19 reviews and 22 protocols registered with the breast cancer group on the Cochrane Library and these cover all aspects of breast cancer from prevention, early detection and treatment.

Since 2002, the Cochrane Breast Cancer Group have received valuable support and funding from the Commonwealth Department of Health and Ageing via a program to support Australian-based Cochrane Collaboration activities. The current funding will see this support extended until June 2005.

The Cochrane Collaboration is the largest organisation in the world engaged in the production and maintenance of systematic reviews. The reviews are available through the Cochrane Library collection (which is free to Australians) via the internet and CD. http://www.cochrane.org.au/

**Hand-searching activities**

The Cochrane Breast Cancer Group is also responsible for hand-searching for relevant trials in a number of journals. Hand-searching, which is a complementary activity to electronic searching, identifies ‘grey literature’, or those trials that are not indexed in major biomedical databases. Currently two consumer volunteers assist the group with hand-searching.

**Breast cancer group activities and developing countries**

A major focus for the Cochrane Breast Cancer Group and challenge for the future is supporting reviewers from developing countries and integrating their specific resources and information needs to make systematic reviews in breast cancer relevant to these populations. Membership and interest from developing countries has continued to grow, with 28 members representing 10 countries classified as low- or middle-income countries by the World Bank.
**Prospective meta-analysis**

Unlike meta-analyses of existing evidence, in a prospective meta-analysis the component trials (usually randomised controlled trials) are identified and evaluated for eligibility before their results are known. Prospective meta-analyses can therefore help to overcome some of the problems of retrospective meta-analyses by enabling:

- hypotheses to be specified beforehand without knowledge of the results of individual trials
- prospective application of selection criteria
- statements of intended analyses, including subgroup analyses, to be made before the results of individual trials are known.

The CTC is participating in the ongoing [Prospective Pravastatin Pooling project](#), a meta-analysis of three major trials using pravastatin for prevention of cardiovascular disease: LIPID, CARE and WOSCOPS. John Simes and Tony Keech are members of the steering committee.

These trials and several others are part of a larger prospective meta-analysis, the [Cholesterol Treatment Trialists’ Collaboration](#), which is using data from 65,000 patients. Tony Keech is joint coordinator of the collaboration.

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**Forum: ‘Prospective meta-analysis and publication bias’**

The CTC’s systematic review team, in collaboration with the Cochrane Prospective Meta-Analysis Methods Group, conducted a well-attended forum ‘Prospective meta-analysis and publication bias’ in November at the main campus of the University of Sydney.

More than 20 types of bias that can occur in the production and dissemination of medical evidence have been specifically identified. Bias can occur from flaws in the design or conduct of meta-analyses or their constituent trials. Further bias, in the reporting of results, also occurs: some results are not published, or are published late or are not in English; others are overpublished or overcited.

The forum presented a series of thought-provoking talks on detecting and analysing bias and reducing it to improve the validity of trial evidence.

International guest speakers were:

- Jesse Berlin, Professor of Biostatistics and Epidemiology, University of Pennsylvania, USA
- Jon Deeks, medical statistician, Centre for Statistics in Medicine, Oxford, UK
- Jonathan Sterne, Reader in Medical Statistics and Epidemiology, University of Bristol, UK.

The University of Sydney speakers included John Simes, Davina Ghersi, John Keech, Christine Pollicino, Petra Macaskill and Les Irwig.

The forum proved to be very successful, generating support for future such events.

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**Visiting scholars**

The CTC was fortunate to have three visiting international scholars during the year:

- Professor Jessie Berlin from the University of Pennsylvania, USA, spent two weeks working on prospective meta-analysis.
- Dr Merce Marzo, a reviewer from the Cochrane Iberoamericano Centre in Barcelona, Spain, spent 3 months working on Cochrane reviews.
- Seong-Hi Park, PhD, from the Korean Health Insurance Review Agency, spent 6 months with the CTC developing skills in health technology assessment.

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**Collaboration on sentinel node biopsy in breast cancer**

The CTC is part of a group that is developing a protocol for a prospective meta-analysis of the role of sentinel node biopsy in early breast cancer. Data from the SNAC trial (p. 17) and other trials of using sentinel node biopsy in early breast cancer will be used. The group had its first meeting in December.
The CTC houses three specialised registers, administered by the systematic reviews group.

The **Cochrane Breast Cancer Specialised Register** is a continuously growing database of randomised controlled trials and controlled clinical trials relevant to breast cancer. A detailed search strategy has been developed to help identify published and unpublished trials relevant to breast cancer to be incorporated into the register. The search is conducted from a variety of sources including Medline, Embase, Physician Data Query (PDQ), the Cochrane Library and various online trial registers. Trials are also found by hand-searching paper copies of journals. Specifically designed searches can be done that will retrieve trials relevant to systematic review questions for the protocols registered with the Cochrane Breast Cancer Group. Other bodies, such as the National Breast Cancer Foundation and the Cochrane Cancer network, request searches for various projects. In 2003, the specialised register had a dramatic increase in the number of trials, and with the addition of international and local hand-searchers, it will continue to grow at a rapid rate throughout 2004.

The **National Clinical Trials Registry** was established in 1995 with the support of Cancer Trials NSW. The aim of the registry is to provide a complete and comprehensive catalogue of clinical trials in cancer in which Australians are participating. It allows searchers to identify unpublished and ongoing cancer clinical trial research and is a compendium for all those with an interest in health care research—including health care providers, consumers and funders.

The **National Clinical Trials Registry** continued to grow in 2003 with the addition of many new trials. The annual update process began in December and will continue throughout the beginning of 2004.

The **Perinatal Clinical Trials Registry**, established in 2000, is an initiative of the **IMPACT Network** (a special interest group of the Perinatal Society of Australia and New Zealand) and the CTC. The registry has been established to provide a complete and comprehensive catalogue of perinatal clinical trials being conducted in Australia and New Zealand. The registry includes clinical trials in the areas of pregnancy, childbirth and neonatal health care, ranging from those in the design stage through to those preparing for the publication of results.

In 2003, the registry had a steady increase in the number registered trials. The annual update process of the registry commenced in December and will continue throughout the beginning of 2004.

The CTC continues to develop the **Clinical Trials Data and Information Network**, which is the CTC's generic **clinical trials management and data collection system**. It was made possible by a major grant in 2001 from the Commonwealth Department of Education, Science and Technology, backed up by an equipment grant from the University of Sydney.

The project development team has included full-time analysts and various CTC users. The information services team was increased from 5 to 7 software engineers during the year. Development was challenged by the high functionality required and the need to adopt the Java 2 Enterprise Edition standard for software development.

Most of the common components were developed, and the first module (randomisation, version 1.0) was developed and successfully tested. The CTC’s fledgling venous thrombosis trial, **ASPIRE**, is being used as the test area.

User specifications for drug management and electronic clinical report forms have been created by the business analysis team, and will be developed by the information services group in 2004.
One of the CTC’s research interests is in developing prognostic models to identify patients at high risk, to help guide clinical decision making. A patient at high risk may require more treatment and is more likely to benefit from an appropriate treatment. Such patients should be considered for new interventions and trials of new treatment.

The large databases of the CTC’s trials provide data for developing and validating these models of risk of cardiovascular disease. An example of this is the current use of HERO-2 trial data to create a risk model with international application: HERO-2 was a trial of antithrombosis therapy for acute myocardial infarction with patients from Australasia, North and South America, Asia, Europe and Russia.

Another example is the use of the LIPID database for models of stroke risk. In the LIPID study, patients from Australia and New Zealand have so far been followed up for at least 10 years. During the first 8 years, nearly 500 people suffered a stroke. Prediction of the risk of stroke in other populations can be modelled from the data.

SNAC is a multicentre trial comparing sentinel node biopsy with axillary clearance for women with early breast cancer (p. 17). The quality-of-life assessments of the first 500 women randomised are being used to test the validity of the quality-of-life questionnaires used. Of the 500, 98% completed their forms before axillary surgery and 99% completed them a month afterward, providing an excellent basis for the validity study and for measuring their wellbeing during this time.

The multiple risks of patients in clinical trials complicate the statistical analysis of the results. In a cancer clinical trial, for example, an investigator may wish to estimate the efficacy of treatments by comparing patients’ survival in the two arms of the trial. However, the patients may also die from other causes. Estimating patients’ survival requires statistical models that measure the risks of different events; when the risks of different events are dependent on each other (competing risks), the models must account for this. Biostatisticians are analysing these risks in simulation studies in order to arrive at the best models of survival in these situations.

In the design of clinical trials, randomisation is fundamental, but also balancing the treatment allocation across important strata improves the efficiency of the final comparisons. Randomisation
STAFF ACTIVITIES
PEOPLE WORKING AT THE CTC

Directors

John Simes, BSc(Med) (Hons) Syd, M B BS (Hons) Syd, M D Syd, SM Harvard, FRACP, director and senior principal research fellow, co-director of cancer trials
Anthony Keech, M B BS M onash, M Sc Lond, FRACP, deputy director and senior principal research fellow
Wendy Hague, M B BS NSW, M BA UTS, director, Clinical Trials Program, and research fellow
Dorothea Sophia, BEd Deakin, GCM AGSM, business director

Cancer trials

Martin Stockler, M B BS (Hons) UNSW, MSc Toronto, FRACP, cancer trials co-director and senior lecturer
Burcu Cakir, BSocSci(Hons) UNSW, MPh UNSW, oncology program trials coordinator
Haryana Dhillon, BSc Syd, MA Syd, oncology development manager
Sonia Yip, BSc (Hons) Syd, PhD UNSW, associate program manager
Xanthi Coskinas, BSc (N urs) Syd, Grad Dip Psychol Syd, study coordinator
Blair Dickman, BSc Otago, Grad Dip Bioethics Otago, study coordinator
Helen Dodd, BSc Griffith, Grad Dip Clin Biochem Griffith, MPh Griffith, PhD Qld, study coordinator
Priya Duggal-Beri, BBiotech Flinders, PhD Adelaide, study coordinator
Amanda Erratt, Assoc Dip Med Record Admin Cumb, study coordinator
Alpana Ghadge, BSc Bombay, M Sc Bombay, PhD Bombay, GradCert TradeM arkS Law Pract Syd, study monitor
Caroline Greig, BS W’gong (to M ar), data manager
Ellen Harrod, BA Cornell, Grad Dip Psychol Syd (from D ec), data manager
Amanda Kerr, BSc (Psych) (Hons) UNSW, data manager
Elizabeth Knight BSc James Cook, M PH W’gong (from Apr), study coordinator
Sarah Krapf, BSc Tas, data manager
Pip Marks, BSc Syd, data manager
Anne McCall, BSc(Hons) Qld, M Sc Qld, study coordinator
Stephanie Nelson, BAppSci (Phy) Syd, BA (Comm) UTS, study monitor
Alison Pearce, BAppSci UWS, study monitor
Julie Poulter, administrative assistant (from Sep)
Adam Ray, study coordinator (to M ar)
Katherine Sen, BSc La Trobe, study monitor

Clinical data management

Susan Wonders, BDS Syd, head
Claire Monro, BA Syd, data systems developer

Site management

Kathleen Scott, BSc (Hons) Strathclyde, PhD Glasgow, head (from Apr)

Randomisation

Andrew O’C allaghan, BSc (Hons) Oxford, head

ASPIRE trial

Lara Fitzgerald, BSc UWA, Dip HlthSci UNE, project manager
Megan Hay, BM edSci (Hons) Syd, clinical trial assistant

INIS trial

Anne Cust, BSc Qld, BA Qld, M PH (Hons) Syd, project manager
Megan Hay, BM edSci (Hons) Syd, clinical trial assistant
FIELD trial

Elizabeth Keirnan, BScAgr Syd, BA Syd, M Mgt UWS, project manager
Sarah Blakesmith, BSc (Hons) Syd, PhD Syd, clinical trial coordinator
Claudia Anderson, BAppSci (Orthop) (Hons) Syd, DOBA, study coordinator (from Oct)
San Chan, administrative assistant
Stefan Czyniewski, BM edSci Syd, clinical trial associate
Samir Doshi, BCom Mumbai, DipBusAdmin Mumbai, MIB Syd, finance manager (from Jun)
Arnie Dupuy, BBus QUT, finance officer (to Jun)
Kew Flood, clinical trials assistant
Sonja Gillies, clinical trials assistant
Zaved Hossain, BSc (Biotech) UNSW, data manager
Li Ping Li, BM ed China, GradCertDM, safety and outcomes officer
Tracy Matthews, administrative assistant
Faith Papuni, administration team leader

Clinical trials registers

Davina Ghersi, AssocDip Cumb, BAAppSci Cumb, MPH Syd, coordinator

Systematic reviews

Davina Ghersi, AssocDip Cumb, BAAppSci Cumb, MPH Syd, director, systematic reviews, and research fellow
Sue Carrick, RN , M HlthSci Syd, program manager, Cochrane reviews
Sally Lord, MB BS Syd, DipPaed UNSW, FRACGP, epidemiologist and research fellow
Elizabeth barr, BAppSci (Pod) La Trobe, GradDip Pod La Trobe, M PH Syd, project officer
Josephine Belcher, BSc(Hons) UNSW, M MedSci (Clin Epi) Newcastle, project officer
Kristina Coleman, BM edSci(Hons) Syd, PhD Syd, project manager
Nicole Davis, BSc(Hons), W'gong, project officer
Megan Evans, BAppSci (HIM ) Syd, research assistant
Melina Gattelari, BSc (Hons) UNSW, M MedSci (Clin Epi) Sydney, project officer
Mary Lewicka, BSc(Hons) W'gong, research assistant
Luke M arkovich, BA(Hons) M urdoch, project officer
Sharon Parker, RN, BH Sci CSU, M PH (Hons) Syd, assistant review group coordinator
Kelly Rochow, BA (Hons) Newcastle, BAppPsycho Newcastle, project officer
Elizabeth Weir, BH HlthSci Sydney, project officer
Sally Wortley, BH HlthSci(Hons) Sydney, M PH Sydney, project officer

Education

Gemma Ritchie, DipEd Aust Cath Univ, BA M acq, BA (Hons) W'gong, manager, education program
Jackie Brighton, BAppSci UTS, M PH Sydney, education officer
Astrid Hexsel, BBusAdmin Brazil, MIT CSU, training officer (to Jul)
Biostatistics and consulting

Val Gebski, BA UNSW, M Stat UNSW, principal research fellow and senior statistician
Karen Byth, BSc (Hons) Qld, M Sc Qld, PhD Lond, D I C Lond, C Stat RSS, senior biostatistician
Peta Forder, BSc (Hons) Griffith, M PH Qld, statistician
Stephane Hertier, M Math Grenoble, M BA Geneva, PhD Geneva (from Sep), senior biostatistician
Carol Hargreaves, BSc(Hons) S Africa, M Sc S Africa, H D E S Africa, PhD S Africa, M BA Wales, statistician
Malcolm Hudson, BSc (Hons) UNSW, PhD Stanford, professor and principal research fellow
Erica Jobling, executive officer, Biostatistics Collaboration of Australia
Adrienne Kirby, BSc (Hons) Qld, M Sc Syd, senior biostatistician
Rachel O’Connell, BM ath Newcastle, M M edStat Newcastle, statistician
Avinesh Pillai, BSc Auckland, M Sc(Hons) Auckland, statistician
Christine Pollicino, BEc Newcastle, M M edStat Newcastle, statistician

Clinical Trials and Data Information Network

Sue Stewart, M Sc W’gong, GradCertFinAcc UTS, BAAppSc RM IT, project logistics manager
Astrid Hessel, BBusAdmin Brazil, M I T CSU, business analyst
Sarah Mulray, BA MA c q, business analyst
Rebecca Murray, BIS Newcastle, business analyst

Quality-of-life studies

Vlatka Duric, BSc (Hons) Qld, M Psychol Syd, clinical psychologist and associate lecturer

Cost-effectiveness evaluation

Simon Eckermann, BEc (Hons)(M athCompSci) Adel, BSc Adel, Grad Dip HealthEcon Tromso, research fellow

Quality assurance

Gemma Ritchie, DEd Aust Cath Univ, BA MA c q, BA (H ons) W’gong, quality assurance manager
Phillipa Smith, BPharm (H ons) Syd, M Sc Syd, adviser
Elizabeth Knight BSc James Cook, M PH W’gong, project officer (to M ar)

Business administration

Dorothea Sophia, BEd Deakin, GCM AGSM, business director
Cynthia Carr, BEd(AdEd), H RD, human resources manager
Bebe Sim, M Acc CSU, CPA, finance manager
Joseph Bower, administrative assistant
Samir Doshi, BCom M umbai, DipBusAdmin M umbai, M I B Syd, FIELD study finance officer (from Jun)
Amie Dupuy, BBus QUT, FIELD study finance officer (to Jun)
Margaret Edwards, personal assistant to the director
Maki Joseph, Di pEd, finance officer
Joyce Micalef, administrative officer
Faith Papuni, personal assistant to the deputy director
Doris Rattos, administrative assistant
Sarah Verschoore, administrative assistant (from Jul)

Publications

Rhana Pike, BA MA c q, GradCertPsychother Syd, M A Syd, ELS, publications officer
Information systems

Paul Vlagsma, BSc (Hons) Tas, MSc ANU, PhD ANU, information systems manager
Jon Barnett, BE (Hons) UTS, MEng UTS, software engineering manager (from Dec)
Anne Foy, BSc (Comp) MSc, software engineer, oncology
Jianpeng Gu, MCompSci MSc, software engineer, FIELD trial
Paul Hayden, BSc (Hons), software engineer
Mustapha Kara-ali, BE UNSW, MBiomedEng UNSW, software engineer
Jaime Marquez, BS(Eng), software engineer, oncology
Eranga Nanayakkara, BCompSci Syd, software validation officer, CTDIN
Anh Tai Nguyen, BM ath W’gong, database administrator and senior programmer
Ashaar Riaz, BSc (ElectEng) UNSW, MCompSci UNSW, software engineer
James Robson, BSc (Hons) Syd, MCompSci UNSW, software engineer
James Stepien, computer systems officer
Dinh Tran, BM ath W’gong, network administrator
Liem Tran, BM ath W’gong, GradDipCompSci MSc, computer systems officer
Rosie Wang, BM ed China, BSc Otago, MHealthSci Otago, software engineer, CTDIN
Bei Zhong, MCompSci MSc, software engineer, FIELD trial

Research student

David Burgess, BM ed Newcastle, FRACP

Academic staff

John Simes, BSc (M ed) (Hons) Syd, M BBS (Hons) Syd, MD Syd, SM Harvard, FRACP, senior principal research fellow and professor
Anthony Keech, MBBiomed Eng, MSc Lond, FRACP, senior principal research fellow and associate professor
Karen Byth, BSc (Hons) Qld, MSc Qld, PhD, DICT Lond, CStat RSS, lecturer
Vlatka Duric, BSc (Hons) Qld, M Psychol Syd, associate lecturer
Simon Eckermann, BEc(MathCompSci) (Hons) Adel, BSc Adel, GradDipHealth Econ Tromso, research fellow
Val Gebski, BA UNSW, MStat UNSW, principal research fellow and associate professor
Davina Ghersi,.AssocDip Cumb, BAppSci Cumb, MPhil Syd, research fellow
Wendy Hague, MBBiomed Eng, MB UTS, research fellow
Stephane Heritier, MMath Grenoble, MBA Geneva, PhD Geneva, senior lecturer
Malcolm Hudson, BSc (Hons) UNSW, PhD Stanford, professor and principal research fellow
Sally Lord, MBBiomed Eng, DIPPaed UNSW, FRACP GP, research fellow
Anna Nowak, MBBiomed Eng, UWA, PhD UNSW, FRACP, postdoctoral research fellow
Martin Stockler, MBBS (Hons) UNSW, MSc Toronto, FRACP, senior lecturer

The finance group: Bebe Sim, Samir Doshi, Maki Joseph
Academic teaching

**John Simes**
Decision analysis, Master of Public Health and Master of Medicine, University of Sydney
University of Sydney medical program
Medical oncology clinical training, Royal Prince Alfred Hospital

**Anthony Keech**
Controlled clinical trials, Master of Public Health and Master of Medicine, University of Sydney
University of Sydney graduate medical program
Cardiology training, Royal Prince Alfred Hospital
Clinical tutor, Royal Prince Alfred Hospital

**Sue Carrick**
Sociology and politics of health care, Faculty of Nursing, University of Sydney

**Burcu Cakir**
Evidence-based medicine, University of Sydney medical program
Basic sciences in oncology series, NSW Cancer Council

**Vlatka Duric**
University of Sydney graduate medical program
Cancer Trials NSW, orientation training for oncology data managers and study nurses

**Simon Eckermann**
Decision analysis, Master of Public Health and Master of Medicine, University of Sydney

**Peta Forder**
Controlled clinical trials, Master of Public Health and Master of Medicine, University of Sydney

**Val Gebski**
Basic sciences in oncology, NSW Cancer Council
Experimental design and controlled clinical trials, Master of Public Health and Master of Medicine, University of Sydney
Controlled clinical trials, Biostatistics Collaboration of Australia (coordinator)

**Davina Ghersi**
Advanced clinical data management, University of Sydney (subject coordinator)
Evidence-based medicine, Graduate Medical Program, University of Sydney

**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, Biostatistical Collaboration of Australia (coordinator)

**Sally Lord**
University of Sydney graduate medical program

**Anna Nowak**
University of Sydney graduate medical program

**Rachel O’Connell**
Controlled clinical trials, Master of Public Health and Master of Medicine, University of Sydney
Principles of statistical inference, Biostatistical Collaboration of Australia
Martin Stockler
Evidence-based medicine and oncology, University of Sydney medical program
Medical oncology clinical training, Royal Prince Alfred Hospital
Quality of life in oncology, Cancer Council NSW
Making sense of cancer trials, Cancer Council NSW
Patient-based measures, Master of Medicine, University of Sydney (course coordinator)
Clinical epidemiology for physician trainees, Royal Prince Alfred Hospital
Critical appraisal of literature for physicians, Westmead Hospital

Research supervision

John Simes
Daveina Ghersi, Doctor of Philosophy
Wendy Hague, Doctor of Philosophy

Malcolm Hudson
Stephen Brown, Doctor of Philosophy
Piea Peng Lee, Doctor of Philosophy
Catherine Rytmeister, Doctor of Philosophy
David Warton, Doctor of Philosophy

Anthony Keech
David Burgess, Doctor of Philosophy
Gemma Ritchie, Doctor of Philosophy

Val Gebski
Goran Hu, Doctor of Philosophy
Mark Jones, Doctor of Philosophy
Bee Choo Tai, Doctor of Philosophy

Martin Stockler
Vlatka Duric, Doctor of Philosophy
Paul Glare, Master of Medicine
Mark Haran, Master of Medicine
Nick Pavlakis, Master of Medicine
Alison Salkeld, Bachelor of Medical Science

Degrees completed in 2003

Elizabeth Barr: Master of Public Health
Anna Nowak: Doctor of Philosophy, University of Western Australia: The effects of gemcitabine on antigen-specific anti-tumour immunity in a murine tumour model.
Bebe Sim: CPA program

Degrees in progress

Kristina Coleman: Graduate Diploma in Public Health
Blair Dickman: Master of Public Health
Simon Eckermann: ‘Examining hospital performance: the right methods and finding the right level’, Doctor of Philosophy
Peta Forder: Master of Biostatistics
Daveina Ghersi: ‘Rating the quality of clinical trials research using information contained in the research protocol’, Doctor of Philosophy
Mary Ellen Harrod: ‘Physiological and Behavioural Correlates of behavioural activation and inhibition’, Doctor of Philosophy
Elizabeth Keirman: ‘Psychiatry and postmodernism’, Doctor of Philosophy
Sarah Krapf: Master of Public Health
Sally Lord: Master of Epidemiology
Luke Marinovich: Doctor of Psychology
Pip Marks: Master of Public Health
Kirsty Mehalski: ‘Muscle fat metabolism in exercise by 1H NMR spectroscopy’, Doctor of Philosophy
Clare Monro: Graduate Diploma in Computing Science
Eranga Nanayakkara: Master of Business Administration
Tony Keech

ASEANZ cardiovascular and lipid forum advisory board
Asian-Pacific Society of Atherosclerosis and Vascular Disease Prevention executive committee (APSAVD) (founding member and treasurer)
Asia-Pacific Study on CHD Risk Factor Intervention (ASPAC) management committee (principal investigator and study chairman)
BLISS study safety and data monitoring committee (chair)
Cardiac Society of Australia and New Zealand clinical trials working group scientific committee (chairman)
Cholesterol Treatment Trialists’ Collaboration (joint coordinator and convenor)
Department of Health and Ageing medical services advisory committee supporting committee
Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) management committee (principal investigator and study chairman), ANZ recruitment working party, ophthalmology substudy committee, scientific substudies committee, cost-effectiveness substudies committee
ISIS Trials Group steering committee
Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID) study management committee, executive, and quality assurance subcommittee
National Heart Foundation (NSW) Heart Week hospital campaign committee, public campaign committee
National Heart Foundation (NSW) working party on guidelines for cardiac rehabilitation
NHMRC Clinical Trials Centre management review committee and scientific advisory committee
NHMRC project grants committee
National Breast Cancer Centre clinical update editorial committee
Percutaneous Coronary Angioplasty versus Thrombolysis (PCAT) collaborative group (co-coordinator)
Prospective Pravastatin Pooling (PPP) project international steering committee
Virtual Coordinating Centre for International Collaborative Cardiovascular Research (VIGOUR) statistical group (chair) and a VIGOUR leader

External committees

John Simes
ANZ Breast Cancer Trials Group scientific advisory committee
Australasian Cochrane Centre scientific advisory committee
Australasian Gastro-Intestinal Trials Group (AGITG) scientific advisory committee
Cholesterol Treatment Trialists Collaboration (joint coordinator)
Cochrane Breast Cancer Group, coordinating editor
Current Controlled Trials editorial board
Department of Health and Aged Care Medicare services advisory committee (MSAC)
Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) management committee, executive, audit subcommittee (chair), and cost-effectiveness subcommittee
Hirulog Early Reperfusion Occlusion (HERO-2) international steering committee and executive
International Breast Cancer Intervention Study (IBIS-II) international steering committee
Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID) management committee, executive and cost-effectiveness subcommittee (chairman)
NHMRC clinical trials and large-scale grants committee
NHMRC Clinical Trials Centre management review committee and scientific advisory committee
NHMRC project grants committee
National Breast Cancer Centre clinical update editorial committee
Percutaneous Coronary Angioplasty versus Thrombolysis (PCAT) collaborative group (co-coordinator)
Prospective Pravastatin Pooling (PPP) project international steering committee
Virtual Coordinating Centre for International Collaborative Cardiovascular Research (VIGOUR) statistical group (chair) and a VIGOUR leader

Tony Keech

ASEANZ cardiovascular and lipid forum advisory board
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Asia-Pacific Study on CHD Risk Factor Intervention (ASPAC) management committee (principal investigator and study chairman)
BLISS study safety and data monitoring committee (chair)
Cardiac Society of Australia and New Zealand clinical trials working group scientific committee (chairman)
Cholesterol Treatment Trialists’ Collaboration (joint coordinator and convenor)
Department of Health and Ageing medical services advisory committee supporting committee
Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) management committee (principal investigator and study chairman), ANZ recruitment working party, ophthalmology substudy committee, scientific substudies committee, cost-effectiveness substudies committee
ISIS Trials Group steering committee
Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID) study management committee, executive, and quality assurance subcommittee
National Heart Foundation (NSW) Heart Week hospital campaign committee, public campaign committee
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NHMRC Clinical Trials Centre management review committee and scientific advisory committee
NHMRC project grants committee
National Breast Cancer Centre clinical update editorial committee
Percutaneous Coronary Angioplasty versus Thrombolysis (PCAT) collaborative group (co-coordinator)
Prospective Pravastatin Pooling (PPP) project international steering committee
Virtual Coordinating Centre for International Collaborative Cardiovascular Research (VIGOUR) statistical group (chair) and a VIGOUR leader
Virtual Coordinating Centre for International Collaborative Cardiovascular Research (VIGOUR)

**Vlatka Duric**
Cancer Council NSW, trial selection committee
European Organisation for Research and Treatment of Cancer quality of life group—gynaecology

**Val Gebski**
ANZ Breast Cancer Trials Group scientific committee
ANZ Breast Cancer Trials Group trial ANZ 9311 management committee
Australasian Gastro-Intestinal Trials Group (AGITG) IG9801 management committee
Australasian Gastro-Intestinal Trials Group (AGITG) scientific committee
Joint Radiation Oncology Centre research committee
Medical Journal of Australia statistical editor
N MRC Singapore Indomethacin study for closure of PDA safety data and monitoring committee
N MRC Singapore trial SHN 01 safety data and monitoring committee
NSW Health Eastern Sydney Area ethics committee—clinical trials subcommittee
Sentinel Node Biopsy vs Axillary Clearance (SNAC) trial management committee

**Davina Ghersi**
Cochrane Collaboration international steering group, executive, colloquium policy committee, electoral process committee, advisory group, Specialised Registers Development Project, prospective meta-analysis methods group (co-convenor), advisory board for the editorial process for Cochrane methodological reviews, international advisory committee, 12th Cochrane Colloquium, Cochrane Breast Cancer Group editorial committee
Association for Clinical Data Management international collaboration subcommittee
Course advisory committee, Master of Health Science and Graduate Certificate in Health Science, University of Sydney
University of Sydney evidence-based medicine resource group
ZEST Trial management committee (chair)

**N SW** Cancer Council Cancer Trials NSW trial selection committee
N SW Health Pilot Shared Scientific Assessment Scheme reference group

**Wendy Hague**
Aspirin to Prevent Recurrent Venous Thromboembolism (ASPIRE) executive
International Neonatal Immunotherapy Study (INIS) Australian and New Zealand management committee
Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) executive, management committee

**Elizabeth Knight**
Australian Health Research Data Managers Association executive committee

**Pip Marks**
Australian Health Research Data Managers Association educational subcommittee (secretary)
School of Health Information Management, University of Sydney, external advisory committee

**Anna Nowak**
Cancer Council NSW, trial selection committee
Cancer Council NSW, centre selection committee

**Martin Stockler**
Cancer Trials NSW Trial Selection Committee (chair)
ANZ Breast Cancer Trials Group protocol 0001 management committee (study chair)
Cochrane Breast Cancer Group
Good Prognosis Germ Cell Trial management committee
ISource National Breast Cancer Centre medical oncology advisory group
NSW Cancer Control Network governing committee
NSW Cooperative Oncology Group (chair)
Pilot phase II study of sandostatin LAR in patients with advanced hepatocellular carcinoma management committee
Trans-Tasman Radiation Oncology Group (TROG) and the Australasian Gastro-Intestinal Trials Group (AGITG) protocol IG9401 management committee
University of Sydney evidence-based medicine resource group
PUBLICATIONS

Journal articles


**Reports**


**CTC collaborative groups**


PROGRESS Collaborative Group [Simes J*]. Effects of a perindopril-based blood pressure lowering regimen on cardiac outcomes among patients with cerebrovascular disease. European Heart Journal 2003; 24: 475–484. *Data Monitoring Committee

Peer-reviewed abstracts


Carrick S. Incorporating time-to-event data in Cochrane reviews using the hazard ratio. 11th Cochrane Colloquium: Evidence, Health Care and Culture; 26–31 Oct 2003; Barcelona.


Duggal PS, Dalla-Pozza L, McCahon E. ANZCCSG study B: progress. Australia and New Zealand Children's Cancer Study Group 17th Annual Scientific Meeting; 19–22 Jun 2003; Sydney.

Duric V, Sharpe L, Stockler M, Butow P, Dhillon H, Boyle F, Sullivan A, B eth J, Wlicken N. Psychosocial predictors of decisions about adjuvant chemotherapy among women with early breast cancer. 6th World Congress of Psycho-Oncology; 23–27 Apr 2003; Banff, Canada.


Ghersi D, Beller E. A problem-based learning approach to the post-graduate teaching of clinical data management. Controlled Clinical Trials 2003; 24: 119S–119S.


Keech AC, Colquhoun DC, Kirby AC, Best J, Simes RJ, for the LIPID investigators. Metabolic syndrome, best identified by obesity and dysglycemia, is associated with greater benefits of pravastatin in patients with coronary disease: the LIPID trial. 76th Annual Scientific Sessions of the American Heart Association; 9–12 Nov 2003; Orlando.


Lord SJ, Mack WJ, Van Den Berg D, Pike MC, Inglis SA, Haiman CA, Wang W, Parisky Y, Hodis HN, Ursin G. Genetic variants that predict mammographic density changes in postmenopausal hormone therapy users. SNPs, Haplotypes, and Cancer: Applications in Molecular Epidemiology; 13–17 Sep 2003; Key Biscayne, Florida, USA.


Nowak AK, Stockler MR, Byrne MJ. Use of the EORTC QLQ-C30 and LC13 in a study of combination chemotherapy for pleural malignant mesothelioma: feasibility, validity and baseline H RQL. Medical Oncology Group of Australia Annual Scientific Meeting; 13–16 Aug 2003; Canberra.


Stockler MR, Tattersall MHN, Boyer MJ, Clarke SJ, Beale PF, Simes RJ. Improving predictions and discussion of survival time in people with incurable cancer: Making the prognosis less guarded. American Society of Clinical Oncology; 31 May-3 Jun 2003; Chicago, USA.


Vardy J, Stockler M, Pillai A, Warr D. Acetaminophen (paracetamol) improves pain and overall well-being in people with advanced cancer already on a strong opioid regimen: A randomized, double-blind, placebo-controlled, cross-over trial. American Society of Clinical Oncology; 31 May-3 Jun 2003; Chicago, USA.


Invited presentations

Cakir B. A plan for a research workshop for registrars in the department of radiation oncology. Trans-Tasman Radiation Oncology Group Data Managers Workshop and Annual Meeting; 12 Mar 2003; Canberra.

Ghersi D. Encouraging consumer participation in Cochrane reviews. Aspects of Evidence Symposium (Australasian Cochrane Centre); 29 Mar 2003; Melbourne.


Nowak A. What makes chemotherapy worthwhile in early colorectal cancer? AGITG Annual Scientific Meeting; 15–17 Aug 2003; Canberra.

Nowak A. Secondary prevention of hepatocellular carcinoma. AGITG Annual Scientific Meeting; 15–17 Aug 2003; Canberra.


Stockler MR, Tattersall MHN, Boyer MJ, Clarke SJ, Beale PF, Simes RJ. Improving predictions and discussion of survival time in people with incurable cancer: Making the prognosis less guarded. American Society of Clinical Oncology; 31 May–3 Jun 2003; Chicago, USA.


Vardy J, Stockler M, Pillai A, Warr D. Acetaminophen (paracetamol) improves pain and overall well-being in people with advanced cancer already on a strong opioid regimen: A randomized, double-blind, placebo-controlled, cross-over trial. American Society of Clinical Oncology; 31 May–3 Jun 2003; Chicago, USA.


Invited presentations

Cakir B. A plan for a research workshop for registrars in the department of radiation oncology. Trans-Tasman Radiation Oncology Group Data Managers Workshop and Annual Meeting; 12 Mar 2003; Canberra.

Ghersi D. Encouraging consumer participation in Cochrane reviews. Aspects of Evidence Symposium (Australasian Cochrane Centre); 29 Mar 2003; Melbourne.


Nowak A. What makes chemotherapy worthwhile in early colorectal cancer? AGITG Annual Scientific Meeting; 15–17 Aug 2003; Canberra.

Nowak A. Secondary prevention of hepatocellular carcinoma. AGITG Annual Scientific Meeting; 15–17 Aug 2003; Canberra.