The Australian Clinical Trials Alliance: Progress & Plans

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VIC Dept of Health: Streamlining Clinical Trials Research Forum
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Disclosures

› Cancer Trials Australia (CTA)
› Australian Clinical Trials Alliance (ACTA)
› Cancer Drugs Alliance (CDA)
› Australasian Gastro-Intestinal Trials Group (AGITG)
› Pharmaceutical Advisory Boards
Overview

- The value of investigator-led networks & “public-good” clinical trials
- Formation of the Australian Clinical Trials Alliance (ACTA)
- ACTA’s Progress and Plans
The value of investigator-led networks & “public-good” clinical trials
Many clinical decisions in medicine are based either on low quality or minimal evidence.

Very significant research conducted in Australia has (regularly) demonstrated that therapies in widespread use, were either ineffective or harmful.

Investigator-led networks are an effective and cost-effective mechanism to undertake important public-good research.
The role of investigator-led clinical trials networks

- Test interventions with clinical but not necessarily commercial relevance “Public-Good Trials”
  What are the clinically important questions?

- Help define the standard of care

- Engage a multidisciplinary group of stakeholders in that field of medicine/disease state

- Identify components of standard care that are harmful or ineffective
The role of investigator-led clinical trials networks

› Define new uses for old drugs

› Evaluate processes-of-care, strategies of care and parallel vs intersecting interventions

› Develop clinical trials capacity and expertise within hospitals and health services

› Augment the capacity of clinical registries to improve quality of care
Networks can do these trials on a sustainable basis

- Access to sufficient sample size
- Create infrastructure once
- Create culture of research
- Corporate knowledge
  - Trial design, project management, data management, trial conduct, pragmatic entry criteria and data requirements
Network strengths

› Run by clinicians who understand what is relevant to clinicians

› Ownership models - self / society / college
  – Responsible to and representative of members

› Mentor and train next generation

› Effectively collaborate with similar international networks

› Translation of research into practice
  – Community of clinicians who are invested in trial results
Clinical trials networks in Australia

38 established; 8 in development (being updated)
Clinical trials networks in Australia

› Still establishing all of the current clinical trial networks and those still in development

› Some debate as to how to define a clinical trial network since any investigator-initiated trial involving multiple sites requires a network of like-minded investigators for its success

› Many examples of investigator-initiated trials that have been practice changing based on new evidence of effective new therapies or ineffective standard therapies...
Practice-changing trials: Anaesthesia

- ENIGMA Trial of 7,000 patients showed that avoiding nitrous oxide during surgery reduces serious post-operative complications by 20-30%.

- MASTER trial of 900 patients having major surgery identified clear pain control benefits of epidural block but no evidence of reduced serious complications.

- B-AWARE trial of over 2,000 at risk patients proved that bispectral index monitoring reduced the incidence of “waking up” by 80%.

- POISE Study of over 8,000 patients having major surgery, showed that although beta- blockers reduced heart attacks, there was an unacceptable increased risk of stroke and death after surgery.
DECRA Trial showed that early decompressive craniectomy for patients with severe traumatic brain injury (TBI), doubled the number of patients with severe neurological impairment. Avoiding early DC estimated to save $100M pa in Australia.

NICE-SUGAR Trial of 6000 critically ill patients showed that tight glycaemic control in ICU (global standard of care at the time) increased mortality. These results mean there are now 3 fewer deaths for every 100 patients treated in Intensive Care Units.
Practice-changing trials: Nephrology

- IDEAL Trial studied 828 participants who were randomised to early or late start of dialysis and showed no difference in survival or rates of major adverse events.

- SHARP Study recruited 9,438 participants with chronic kidney disease followed for a mean of 4.9 years to examine the effect of cholesterol lowering upon major cardiovascular events. The study demonstrated a 17% reduction in major atherosclerotic events.

- RENAL Trial recruited 1,508 participants to a trial of augmented versus normal intensity of continuous renal replacement therapy in people with severe acute kidney injury found no difference in 90-day mortality or requirement for ongoing renal replacement therapy. Resulted in significant cost-savings to the health system.
A large international trial demonstrated that the generic drug tamoxifen could reduce by 1/3 the incidence of breast cancer in women at high risk of developing the disease.

HERA trial demonstrated the effectiveness of trastuzumab (Herceptin) in reducing recurrence and improving survival in women with a high-risk form of early breast cancer.
Links with Industry

- Shared infrastructure for conducting research
- Shared need to building research capacity and expertise
- Shared incentives to develop efficient and effective trial processes at a national level
- Shared interest in remaining globally competitive and at the cutting edge of advances in clinical trials
- Shared commitment to understand gaps in the evidence-base and hence to drive reform
A self-improving health system

Cooper et al; Blood CRE Research Strategy
Why do trials here?

AUSTRALIAN TRIAL

DEFINE  TRIAL  ANALYSED  ABSTRACT  PUBLISHED
2014  2015  2016  2017  2018

AUSTRALIAN PRACTICE

DEFINE  TRIAL  RESULTS  CHANGE
TOP GEAR: TRIAL OF PREOPERATIVE THERAPY FOR GASTRIC AND ESOPHAGOGASTRIC JUNCTION ADENOCARCINOMA

A randomised phase II/III trial of preoperative chemoradiotherapy versus preoperative chemotherapy for resectable gastric cancer
Protocol number AG0407GR TROG number 08.08

Version 6, 10 July 2012

Study Chair:
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Topgear trial

Randomise

Chemo

ECC x3

Chemo

ECC x3

Sx

Chemo

ECC x3

Chemo

ECC x2

Chemo

Chemo/XRT

Sx

Chemo

ECC x3

XRT = radiation therapy
Sx = surgery
Conclusion

• Participation and conduct of a clinical trial changes clinical practice independently of any new finding that may result from the trial.
Question?

Does the overall prognosis of patients who participate in randomised clinical trials differ from those treated outside trials who receive “standard treatment”? 
The Trial Effect

• Strong anecdotal argument that patients in clinical trials have better outcomes regardless of which treatment they are allocated to.

• Several systematic reviews with varying levels of evidence but all have reported no negative impact on outcomes of patients who participated in trials.

• Many examples of a positive trial effect at the individual study or institution level.
Breast Cancer Outcome in Clinical Trials

M GNANT Proc ASCO 287 2000
Australian Breast Cancer Study Group

- 7738 patients Stages 1 and 2
- 1980-99; 7 years follow up
- 5773 enrolled in randomised trials
- 1965 standard treatment off study
- 2 groups comparable and very similar
- Comparison of survival
Conclusions

• Participation in clinical trials was associated with improved survival

• Possible reasons- quality control, attention to detail, protocol defined treatment and dose modifications, access to new treatments, motivated doctors, nurses and data managers

• Treatment adherence may be suboptimal outside clinical trials

Gant et al 2000
Formation of the
Australian Clinical Trials Alliance (ACTA)
Objectives

- Articulate the case for improved systems and structural support for clinical trials networks.
- Define the need to make clinical trials an integral part of the health system.
Called for recognition and support of investigator-initiated trials and networks

Foreshadowed establishment of the Australian Clinical Trials Alliance - ACTA
The need to come together

- Highly successful networks in a number of clinical areas
- Host of prominent trials that changed practice, improved outcomes or reduced health spending
- No national body to advise Govt on how to best support the sector
- No nationally coordinated mechanism for linking networks and supporting collaboration
Formation of the Australian Clinical Trials Alliance (ACTA)

› Strong call from the sector arising from the MJA Summit

› Critical need for a coordinated voice to advance investigator-led clinical trials and registries as a core component of high-quality health care delivery

› ACTA will aim to become the national peak body for investigator networks conducting public-good clinical trials

› Leadership shown by VIC – first funding tranche
Interim Executive / Founding Directors

Prof John Zalcberg OAM
Prof Fran Boyle AM
Prof Alan Cass
Prof Geoff Donnan
A/Prof Ross Haslam
A/Prof Carmel Hawley
Prof Tony Keech
Prof John McNeil AM
Prof Paul Myles
Prof John Simes
Prof Steve Webb
A/Prof Nik Zeps
Prof Derek Chew
Prof Mark Harris

Exec Officer- Rhiannon Tate
ACTA’s Membership

- Clinical Trials Networks
- Clinical Trial Coordinating Centres
- Clinical Quality Registries
ACTA’s Mission

To promote effective and cost-effective health care in Australia through investigator-initiated clinical trials that generate evidence to support decision making by health practitioners, policy-makers and consumers.
ACTA’s Vision

› A healthcare system that delivers high quality and cost-effective care through the systematic generation and application of evidence derived from clinical research.

› For clinical research, through both clinical trials and registries, to occur as a routine, integral, and universal component of health care delivery.

› For widespread appreciation and support by consumers, health practitioners, and policy-makers for the critical importance of clinical research in Australia to improve practice and policy.
ACTA’s Vision

› That all patients who require treatment for which there is uncertainty about the most effective therapy have the opportunity to participate in high quality clinical trials.

› That the best evidence informing optimal health care is based on well conducted controlled trials of the effect of interventions on clinically relevant outcomes.
Strategic Positioning – “3 Pillars”

- Connect & support clinical trials networks
- Advance clinical trials in health care
- Improve clinical trials efficiency
Objectives

› advocating the advantages and benefits of investigator-initiated clinical trials to policy makers and the general community;

› raising awareness of the need for, and valuable contributions of, clinical trials networks, coordinating centres and clinical registries that conduct, or support the conduct of investigator-initiated clinical trials;

› bringing focus to common issues impacting the conduct of clinical trials;

› facilitating collaboration among clinical trials networks, coordinating centres and clinical registries;

› coordinating sector-wide communication and consultation with clinician researchers;
Objectives

› providing **expert advice** on investigator-initiated clinical trials to Governments, policymakers and others;

› developing **policy recommendations** for improving the quality and impact of investigator-initiated clinical trials and registries;

› supporting the **development** of new clinical trials networks and clinical registries that conduct, or support the conduct of investigator-initiated clinical trials;

› encouraging **capacity building** for the clinical research workforce;

› promoting **education and training** opportunities for clinician researchers;

› coordinating or supporting projects aimed at improving clinical trials **efficiency**;

› fostering effective **partnerships** between clinician researchers and Governments, policy-makers, health care providers, industry and consumers;

› **Public education** about public-good clinical trials.
Key Stakeholders

ACTA

Hospitals & Health Services
State & Federal Govt
Patient & Consumer Groups
Research Funders
Universities
Medical Research Institutes
Human Research Ethics Committees
Industry
Professional Colleges and Societies
Contract Research Organisations
Regulatory & Statutory Bodies
Health Insurers
Funding

› State-based seed funding (2 years)
  - $200K initial seed funding from VIC Health
  - In principle agreement from WA (pro-rata)
  - Active negotiations with remaining jurisdictions

› Mixed model of consolidation/sustainable funding
Progress and Plans
Progress so far...

- ~ 60 trials networks, registries and coordinating centres now formally part of the ACTA community

- Incorporated not-for-profit public company limited by guarantee.
  - Interim Establishment Period – 12 founding Directors
  - 1-2 year transition to a representative governance model
  - Mixed medical/skills-based Board
  - Large representative Advisory Council
  - Devolved working group model inc. state-based project hubs

- Website and social media presence
  - Twitter
  - Closed LinkedIn group, blog and regular newsletter in development
ACTA Summit 2014, 28-29 March

- First major national initiative and official launch of ACTA
- Officially supported by NHMRC (sponsorship from Bellberry Limited)
- More than 165 participants from 95+ networks, registries, coordinating centres + key opinion leaders
- Presentations can be viewed via the ACTA website.
- Formal report on Summit proceedings and outcomes to be published later this month.
## ACTA Summit Participants

Clinical trials networks, trial coordinating centres & clinical quality registries

- ASPREE Study Group
- Australasian Consortium of Centres for Clinical Cognitive Research
- Australasian Gastro-Intestinal Trials Group
- Australasian Kidney Trials Network
- Australasian Leukaemia & Lymphoma Group
- Australasian Lung Cancer Trials Group
- Australasian Radiopharmaceutical Trials Network
- Australasian Sarcoma Study Group
- Australasian Sleep Trials Network
- Australasian Society for Infectious Diseases Clinical Research Network
- Australasian Stroke Trials Network
- Australia & New Zealand Breast Cancer Trials Group
- Australia & New Zealand Neonatal Network
- Australia & New Zealand Society of Cardiac & Thoracic Surgeons National Cardiac Surgery Registry
- Australian & New Zealand Children’s Haematology/Oncology Group
- Australian & New Zealand College of Anaesthetists Trials Group
- Australian & New Zealand Intensive Care Society Centre for Outcomes & Resource Evaluation
- Australian & New Zealand Intensive Care Society Clinical Trials Group
- Australian & New Zealand Melanoma Trials Group
- Australian & New Zealand Urogenital & Prostate Cancer Trials Group
- Australian Cardiac Procedures Registry
- Australian Epilepsy Clinical Trials Network
- Australian Motor Neuron Disease Registry
- Australian Musculoskeletal Clinical Trials Group
- Australian Primary Care Research Network
- Australian Research Centre for Health of Women & Babies, Robinson Institute.
- Bi-national Colorectal Cancer Audit
- Burns Service of Western Australia
- Centre for Anaesthesia & Cognitive Function
- Centre for Biostatistics & Clinical Trials
- Cooperative Trials Group for Neuro-Oncology
- Epworth HealthCare Clinical Trials & Research Centre
- Multiple Sclerosis Research Australia Clinical Trials Network
- Neuroscience Trials Australia
- NHMRC Clinical Trials Centre
- NSW Better Treatments 4 Kids
- Orygen Youth Health Research Centre
- Paediatric Research in Emergency Departments International Collaborative
- Paediatric Trials Network Australia
- Palliative Care Clinical Studies Collaborative
- Perinatal Society of Australia & New Zealand IMPACT Collaboration
- Primary Care Collaborative Cancer Clinical Trials Group
- Psycho-oncology Co-operative Research Group
- Queensland Centre for Mental Health Research
- Queensland Clinical Trials & Biostatistics Centre
- School of Public Health & Preventative Medicine, Monash University
- South Australian Health & Medical Research Institute
- Spinal Cord Injury Network
- The George Institute for Global Health
- Type 1 Diabetes Clinical Research Network
- Victorian Ambulance Cardiac Arrest Registry
- Victorian Cervical Cytology Registry
- Australian & New Zealand Breast Cancer Trials Group
- Australia & New Zealand Neonatal Network
- Australian & New Zealand Society of Cardiac & Thoracic Surgeons National Cardiac Surgery Registry
- Australian & New Zealand Children’s Haematology/Oncology Group
- Australian & New Zealand College of Anaesthetists Trials Group
- Australian & New Zealand Intensive Care Society Centre for Outcomes & Resource Evaluation
- Australian & New Zealand Intensive Care Society Clinical Trials Group
- Australian & New Zealand Melanoma Trials Group
- Australian & New Zealand Urogenital & Prostate Cancer Trials Group
- Australian Cardiac Procedures Registry
- Australian Epilepsy Clinical Trials Network
- Australian Motor Neuron Disease Registry
- Australian Musculoskeletal Clinical Trials Group
- Australian Primary Care Research Network
- Australian Research Centre for Health of Women & Babies, Robinson Institute.
ACTA Summit – Prominent themes

› Better advocacy for public-good clinical trials/registries
› Share expertise and resources between networks
› More cross-discipline trials
› Pragmatic trial design (inc. registry randomised trials)
› Interaction with policy makers during trial development
› Standard tools (PIS, data definitions, outcome measures)
› Standard costs (inc. how “standard of care” is costed)
› Community awareness and education about trials
› Research about research - understanding what we currently do, why it’s vital, and how we can do it better
Year ahead: Advocacy

› Ongoing advocacy around proposed MRFF
› Sector-wide consolidation and representation
   › NHMRC Research Governance Submission
   › NHMRC Design of a new NEAF Submission
   › IHPA table of standard costs for CTs Submission
› Senate Inquiry on Australia’s Innovation System
› Representation on CTAC
› Representation on IHPA Research Working Group
   › Investigating feasibility of ABF for TTR
   › Part of the National Health Reform Agreement, 2011
› Dept of Industry
   › Steering Group to develop training course for Research Governance
   › RIBG for International Grants
› SCoH
Year ahead: Profiling Networks Project

- National snap-shot survey of all existing networks
- Describe structure and function of networks
- Detailed report on aggregate research activity
  - Major research areas
  - Number and type or studies completed/current/planned
  - Recruitment
  - Funding
  - Interaction with Industry
  - National and international collaboration
  - Consumer engagement
- Understand contribution to total clinical trials effort
- Describe impact on pt outcomes/practice/policy
- Formal collaboration with NHMRC
- Inform future work
  - best-practice models for successful networks
  - point-in-time reporting of trial activity in Aust
Year ahead: Policy development

- Opt-Out Consent Working Group
- Standard of Care Costs in Clinical Trials Working Group
- White Paper on the role and value of investigator-led trials and quality registries to the health system.
Year ahead: Connecting

› 2015 International Clinical Trials Symposium
  › Oct/Noc 2015
  › Supported by NHMRC
  › Major international meeting to explore cutting edge advances in trial methodology and health care policy impacting clinical trials.

› Consumer Engagement
  › Tap into the networks of consumers already engaged with ACTA members
  › Facilitate sharing of experiences of networks in promoting consumer engagement in trials
  › Eg IMPACT Collaboration – Ist parent to be listed as an Associate Investigator on an NHMRC grant for neonatal trial.

› Public awareness and education about the importance of clinical trials
Key Message

Clinical Trials and Clinical Quality registries are:

- essential for improving patient outcomes
- vital for improving the productivity of the healthcare system
- a fundamental responsibility of the healthcare system
“The government has indicated that they are interested in clinical trials.”

Jane Halton PSM: Senate Estimates, June 2014

...watch this space.