NHMRC Clinical Trials Centre

The University of Sydney

McKeon Review 2012

NHMRC CLINICAL TRIALS CENTRE

SUBMISSION

30 March 2012

Level 6, Medical Foundation Building
92–94 Parramatta Road Camperdown , NSW 2050
Tel (02) 9562 5000

Prof John Simes, Director
john@ctc.usyd.edu.au

Executive summary

The following are key principles for the 10-year strategy for medical research in Australia.

1. Australia needs to have an internationally competitive health and medical research industry.
2. Clinical trials must be seen as critical to the health and medical strategy in Australia.
3. Clinical trials research and quality research and development programs must be integrated into practice, culture and performance measures of the Australian health care sector.
4. Building infrastructure for clinical trials and translational research capacity (bench to bedside and back again; translating evidence into clinical practice) is critical to the research effort.

To this end, the NHMRC Clinical Trials Centre submits that the following proposals be considered by the committee

- That clinical trials research becomes an integral part of Australian health service delivery in order to improve health outcomes and clinical practice.
- That the conduct of academic clinical trials (investigator-initiated clinical trials) in Australia be more strongly supported.
- That research networks that link basic sciences research with clinical research and practice be more strongly supported.
- That research networks that promote other multidisciplinary studies be supported
- That current disincentives for the best researchers to undertake research for health be overcome
- That there be ongoing commitment to support the Australian New Zealand Clinical Trials Registry (ANZCTR)
- The the following infrastructure initiatives be established or expanded: early phase clinical trials units; national hub for clinical trials in low cost interventions; national infrastructure support for collecting clinical trial biospecimens and biobanking; national advisory and resources hub for clinical trials; national e-research hub for investigator initiated clinical trials; education and career paths for clinical trials research workforce; clinical trial data and economic modelling be applied to facilitate policy decisions for government, health service administrators and public and private funders

NHMRC Clinical Trials Centre submission

The NHMRC Clinical Trials Centre is pleased to make a submission to the 2012 McKeon Review. This document provides comments and proposals to the Australian Government for optimising the country's capacity to produce world class health and medical research to 2020.

The NHMRC CTC responds to each of the four questions of the McKeon Review as follows:

1. Why is it in Australia's interest to have a viable, internationally competitive health and medical research sector?

A vibrant and productive health and medical research sector brings health benefits to Australians and economic benefits to the country.

Ongoing improvements to health care and more efficient use of treatments and resources in health are likely to bring savings to government expenditure.

With rapid growth in health technologies and population ageing, health care costs in Australia and internationally are increasing. Currently, we spend over $100 billion on health care, and government spending is projected to almost double as a proportion of GDP by 2050. In this environment, we need to ensure that each new and existing health care recommendation and policy is based on sound evidence of cost-effectiveness, and also that our approach to delivering better health outcomes is based on strategies that are smarter and better targeted.

For developing effective treatments and provide high-quality healthcare, an essential component is health and medical research. This research generates information for: improving patient care using new treatments and therapies; improving safety for patients; and more cost-effective care. Australia has an excellent research record and delivers a relatively high output per capita in this area already.(1) In the current climate, where it is to Australia's advantage to be 'thinking and working smart', health and medical research is an area we can further develop and maintain as a world-class industry, in contrast to other industries, such manufacturing, that are becoming increasingly less competitive.

Data arising from solid research,that is,well-designed clinical trials, integrated with translational research generating reliable and robust results are critical to real advances in patient care.(2-5)

A major component of the cost of new treatments is the sharply rising cost of clinical trials. But clinical trial programs have been shown to be much more cost-effective than many of the treatment programs that we accept as value for money.(6) To make the best use of finite health care resources in the future, linking a sophisticated clinical trials research program to other relevant areas is essential. This means incorporating basic sciences and cutting-edge technologies into clinical trials and trial evidence, in turn, to be integrated with other relevant information for its optimal use in informing practice and policy.

2. How might health and medical research be best managed and funded in Australia?

While health and medical research could continue to be managed through the current NHMRC models of funding, the following issues still need to be addressed urgently:

1. Significant additional funds are required to ensure quality and breadth of clinical research and better development of health care in Australia.
2. Ongoing mechanisms that reward excellence in research must be maintained for recognising achievements and to propel improvements in research standards
3. Models for strategic funding linking government, academia, NGOs, industry and relevant stakeholders, which can also leverage funding in priority research areas (for example, therapeutic areas, technology-driven research) must be nurtured and maintained.
4. Funding of public-good and comparative-effectiveness studies directly from the healthcare budget as part of the model to provide high-quality health care.

Role of the clinical trial

A clinical trial is a research study that assesses treatments or health-related interventions in humans to evaluate the effects on health outcomes. Trials can evaluate new or existing drugs, different types of surgery, forms of supportive care or indeed any intervention that might impact on health.

The NHMRC CTC proposes that we ensure clinical trials research is an integral part of Australian health service delivery in order to improve health outcomes and clinical practice.

This can be achieved by:

1. integrating high-quality research and development programs in health care in Australia, including
   i. greater development and implementation of evidence-based health policy
   ii. evaluation of quality of care through controlled trials and evidence-based studies funded from within the healthcare budget
   iii. accreditation and funding of hospitals based on an acceptable level of participation in clinical trials research as an integral part of quality health care delivery. This includes mandatory requirement for hospitals to report the following key performance indicators (KPIs) in annual reports for health managers and clinicians: the number of staff active in research (expressed as full-time equivalents); the number of clinical trials undertaken; the number of patients recruited to trials

   The role of government in ensuring that clinical trials be incorporated into standard health care delivery cannot be understated. In the UK, the Department of Health commenced investing new monies into infrastructure support for clinical trials research in cancer over 10 year ago (National Cancer Research Network) and implemented a government directive for 10% of newly diagnosed patients entering into clinical trials. This successful model has now been

expanded into other therapeutic areas, including cardiovascular disease and diabetes in the UK.

2. building clinical trials research infrastructure to ensure that clinical trials activity in Australia remains globally competitive, by

    i Building local capacity to support multicentre trials, including local research staff to enhance often slow rates of patient recruitment and local administrative staff for efficient compliance with complex regulatory requirements. Both are currently major rate-limiting steps in the conduct of trials.

    ii Further developing strategic alliances and relationships between academic research groups, government and industry, especially in translational research. Partnerships are of value in both: taking new scientific discoveries in to the clinic and new clinical problems to the laboratory, and also improving the quality of care by better translating new clinical evidence into practice and policy. An international model of note is the one in Singapore for translational research, which is set up such that research partnerships are geared bring in new research monies.

3. building on the existing and unique strengths of health and research institutions. Australia has strong medical science and research institutions. For example, NSW has been a national and international leader in clinical trial research through groups including the NHMRC Clinical Trials Centre, the George Institute and the National Centre in HIV Epidemiology and Clinical Research (now Kirby Centre). Medical research institutions in other states include, in Victoria, the Walter Eliza Hall Institute and Peter MacCallum Cancer Institute; and in Queensland, the Queensland Institute of Medical Research. One option is to provide a national hub for trialists to share information and expertise.
4. A change in government policy and influencing cultural attitudes toward promoting and facilitating great philanthropic support for research, as exemplified by the USA. Approaches to make such contributions more attractive to potential philanthropists may include taxation considerations.
5. Further improvements to the current ethical and regulatory guidelines for the establishment and conduct of clinical trials.

The two major categories of clinical trials research are: 1. those devised and coordinated by the pharmaceutical industry for the registration and thus marketing of their new products; and 2. those planned and conducted by clinicians to answer questions of public health importance—these are called investigator-initiated clinical trials research. This distinction is germane because current regulations are based on industry requirements for drug registration, not to inform practice, and the two categories are treated the same, whereas there are key differences, often in types of interventions, study design, level of risk, etc.

6. Many of these studies require hundreds to thousands of patients and so need to be conducted across multiple initiations and sometimes countries. he process needs to streamlined, but without ethical breaches. The national ethics application needs to be accepted by all others with no state- or site-specific additional requirements. Site governance processes should be streamlined to facilitate rapid completion with a

total ideal timeline of 30 days, to be undertaken in parallel with the lead HREC approval.

7. Further rationalisation of safety reporting to HRECs and sites based on the distinction between interventions currently already being used in practice versus new unlicensed products. For pragmatic clinical trials and comparative-effectiveness studies, a simplified and streamlined ethics and regulatory environment is needed, comparable to clinical practice standards for routine care. This will ensure such studies can be truly integrated into quality-improvement activity.

3. What are the health and medical research strategic directions and priorities and how might we meet them?

The strategic directions and priorities should build on the principles outlined in section 2, and in particular support the following specific proposals:

1. Provide greater support for translational research
2. Provide greater support for clinical trial networks for investigator-initiated trials
3. Provide greater incentives for clinicians and health professionals to engage in research
4. Provide ongoing supportfor the Australian New Zealand Clinical Trials Registry
5. Increase support for early-phase clinical trials
6. Invest in low-cost interventions
7. Provide infrastructure support for biotechnology
8. Establish a national research hub for investigator-initiated trials
9. Increase education and career paths for the clinical research workforce

The strategy should ensure support for conduct of academic clinical trials (investigator-initiated clinical trials) in Australia. Clinical trials designed and initiated by investigators often aim to answer important clinical and scientific questions that are not driven by commercial interests, for example

- research using ‘old drugs’ (off-patent) or noncommercial interventions
- therapeutic areas with small patient populations
- therapeutic areas common in developing economies and/or disadvantaged communities

Academic clinical trials complement clinical trial research conducted by industry. There are, however, mutual benefits of a relationship between academic clinical trial researchers and pharmaceutical companies

- Expertise, resources etc. in pharmaceutical and biotechnology companies are geared to early drug development

- Academic research groups in clinical trials may have access to wide patient population networks (especially for rare diseases) not readily available to pharmaceutical companies
- Networks have access to a pipeline of drugs in development (by the pharmaceutical industry) for research in areas of unmet clinical need and complement those clinical areas already prioritised by commercial drug developers.

Academic researchers would benefit from accessing and consulting those with experience working within drug development (in academia and commercial environments), understanding not only the scientific processes and decision making but also the commercial processes, drivers and consequences of decisions made at key points of drug development.

Support for translational research

Funding for research and infrastructure supporting translation of basic scientific research into clinical trials and translational of medical evidence into clinical practice is important.

Translational studies bring together different disciplines to harness latest technologies (for example, next generation sequencing) and develop new trial designs to address clinical and scientific questions as we move to an era of personalised medicine. The research community needs to recognise that funding for translational studies

- often requires a separate grant funding application where not included with the original funding request (from granting body or pharmaceutical company)
- have budgets for expensive technologies that may exceed trial budgets, for example, where the translational study is based on next-generation sequencing

Assisting the NHMRC in Canberra to build their proposed translational research faculty with representation across a broad range of disciplines will be critical in developing a group with strong expertise and experience to guide translational research direction and policy in Australia.

Support clinical trial research networks

Groups include those in oncology, cardiovascular, diabetes, obesity and neonatal, perinatal and paediatric diseases.

Support of scientific and research questions that have maximum impact on future clinical practice and health policy and ultimately translating into better health outcomes. Focus should be on

- disease areas of major mortality and morbidity
- interventions with the potential to affect each disease
- large collaborations in these areas to generate data quickly and efficiently and engage researchers
- further developing methods for assessing and applying clinical trial evidence both to individual patients and to populations at large
- integrating clinical trials research with value-added studies of biomarkers, genetic factors, patients preference, quality of life and health economics

Support for these trials networks includes:

- funding for infrastructure support
- seeking opportunities to obtain or leverage funding from additional programs (international funding bodies, industry)
- attracting and developing specialist expertise in areas including bioinformatics, biostatistics, and health economics
- identifying opportunities where these trials networks can build strategic alliances, within the state, nationally and internationally

Policy and funding changes to enhance opportunities for the best research in health

A range of strategies related to clinical and other researchers are needed to provide greater incentives.

1. Research is often affected by tender conditions owing to short time frames. Longer lead times from tender publication to closing dates would ensure better-quality proposals are submitted.
2. Increases in tier 1 infrastructure funding would improve security and stability for clinical research.
3. Increased funding for mid-career and senior researchers would retain the best researchers.

Australian New Zealand Clinical Trials Registry (ANZCTR): need for ongoing infrastructure funding

The ANZCTR forms one of the key platforms in Australia's national research infrastructure, ensuring Australia takes responsibility for the oversight of health and medical research conducted within its borders, and it helps ensure Australians meet their ethical and international obligations for research transparency.

The ANZCTR is an essential national research infrastructure facility which will underpin the implementation of the recommendations of the Clinical Trials Action Group (CTAG) report by the NHMRC and DIISRTE.(7)

We propose support for the ANZCTR's ability to provide up-to-date and comprehensive information about all clinical trials being conducted in Australia to consumers, health professionals, funders, regulators, researchers, journal editors and other stakeholders.

More early-phase clinical trials units

Phase I clinical trials are first in-human testing of therapies, including new drugs and devices. There is a paucity of phase I expertise and infrastructure in NSW although this state has the largest population to service. While commercial early-phase trial organisations exist in Australia, early-phase trials units in the hospital/academic setting are still needed.

Building more early-phase research capacity would contribute to the Clinical Trials Roadmap set out by CTAG, established by the Australian Government, to develop a strategy for promoting Australia's competitiveness in the clinical trials arena.

Invest in clinical trials of low-cost interventions

Conclusive clinical trials are the standard of evidence required to take proven technologies forward to widespread appropriate use in the human population and, if cost effective, funded by government and health providers. Examples of drugs successfully developed de novo through Australian Government investment include zanamivir (Relenza), an influenza treatment, and Gardasil (HP4), a vaccine for cervical cancer. While high-cost patentable clinical interventions can provide important advances in health care and commercial benefits, it is important to keep in mind that most promising new treatments and technologies prove neither effective nor cost-effective. The costs of insurance and medicolegal risks during de novo drug development must also be taken into account.(8)

There are also substantial gains to be made to be made through low cost interventions which may be highly cost-effective and lead to significant improvements in population health, some with potential savings over current treatment and the flow-on benefits of improved health to other sectors through gains in productivity. Examples of effective, low-cost drugs are: antenatal corticosteroids in threatened preterm delivery,(9) antenatal magnesium sulphate 3, which reduces cerebral palsy in survivors by a third, and tranexamic acid.(10)

Other promising, low-cost, unpatented or out-of-patent interventions for common conditions merit high priority for reliable evaluation in translational research by randomised controlled trials as they provide a safe, potentially cost-effective strategy for advancing health.(11) Investment in the infrastructure and research staff needed in international collaborative networks to evaluate low-cost interventions in large randomised controlled trials is a major priority for translational research. The possibility that such interventions may lead to moderate benefit (or harm) should not be discounted until they have been reliably tested in large randomised controlled trials.(12)

Infrastructure support for collecting clinical trial biospecimens and biobanking

The study of biospecimens (tissue and blood from patients) that are linked to poor or incomplete clinical and pathology datasets has many limitations. In contrast, biospecimens from patients participating in clinical trials (and matched apparently healthy control subjects) provides a valuable biological resource, with linkage to high-quality clinical data. The latter are usually detailed (including information on clinical outcomes) and of high quality (often monitored data). Collection of such rich resources associated with informative clinical datasets must be supported by the Australian research community through adequate funding for prospective collection of biospecimens from clinical trials and related data (now and in the future), including

- costs of laboratory consumables, site costs for collection of biospecimens and related clinical data, central coordinating centre costs
- medium- to long-term storage of biospecimens (likely to be decades for cancer and complications of vascular disease and diabetes), that is, access to biobanking facilities and funding to cover costs of fee-for-service biobanks

While fee-for-service biobanks exist in Australia (commercial and government-funded), they are either out of the price range of academic or investigator-initiated clinical trials (in the case of commercial biobanks), or the medium to long-term viability of government-funded biobanks is uncertain, given the recent withdrawal of ongoing funding for biobanks in Australia (for example, NHMRC enabling grants) . While some academic laboratories have limited capacity to store biospecimens, particularly where they have vested interests in

conducting specific biological research projects, this is clearly not a sustainable option, as the number of clinical trials with prospective collection of biological material increases exponentially, if current trends continue.

A long-term model of collection, storage and access to biospecimens from clinical trials, searchable online by potential research collaborators, under a sustainable funding stream is clearly needed nationally.

1. Physical biobank of clinical trial patient samples

A physical biobank would be a national resource for clinical trial samples across all therapeutic areas, including cardiovascular disease, diabetes and oncology. Biosamples collected would include: fresh tissue, formalin-fixed paraffin-embedded blocks, peripheral blood pellets, serum and plasma (and perhaps saliva as a noninvasive source of DNA).

The central storage of biological samples from clinical trials

- will contribute significantly to the national capacity, allowing long-term safe storage of frozen specimens, allowing access to processing of tissue samples, for example, for microarrays, and facilitate more efficient conduct and coordination of studies as specific projects are identified.
- is linked to clinical trial data and clinical cohorts. This will allow better identification of prognostic and predictive factors. In this regard, linkage of samples to outcomes in randomised trials is especially important.
- allows consolidation of samples for a specific trial before further shipping .

A national biobank for these clinical trial samples would also require resources to fund personnel to manage the biobank, including taking receipt of samples, tracking samples, maintaining a database and retrieving samples for research request.

2. Virtual national biobank of clinical trial patient samples

The purpose of a virtual national tissue bank for clinical trials would be to provide a 'one-stop-shop' where information can be found on the type of biological material (for example, fresh tissue, formalin-fixed paraffin embedded blocks, serum, plasma) and the extent of linked clinical information for that clinical trial patient for samples stored at multiple sites around Australia.

- The virtual national tissue bank website would also contain contact information and how to apply for use the samples for research. This would provide improved information and access to collected biospecimens from clinical trials.
- The virtual biobank would encompass all clinical trial samples collected from all therapeutic areas in Australia.
- This work depends on the support of the particular trial groups responsible for the individual trials and other clinical researchers and practitioners

  To minimise duplication and to promote inclusiveness, the virtual national biobank would be a portal and link up to existing tissue banks and national databases in Australia, for example, the Australasian Biospecimen Network (ABN); BioGrid, Breast Cancer Tissue Bank and Victorian Cancer Biobank.
- **Oncology.** A virtual biobank would encompass samples collected from trials run by the various Australian oncology collaborative groups. There would be the opportunity to

also link to other known oncology tissue repositories around Australia. This is an initiative also supported by translational cancer research networks and international groups.

- **Other therapeutic areas.** A virtual national database would also include information on biological material collected from clinical trials in all other therapeutic areas conducted in Australia. For example, some forms of cancer are more common in people with diabetes.
- A living biobank might allow people who are open to being approached for future studies (for example, as control subjects) to register and provide a blood sample for genotyping.

National e-research hub for investigator initiated clinical trials

Support for a national e-research infrastructure would facilitate and accelerate investigator-initiated clinical trials across Australasia and beyond.

This infrastructure would use technology to leverage the expertise and experience of existing academic trial organisations and groups, employing collaboration tools and other systems to bring about an unprecedented level of shared resources, templates, and best practices. A centralised resource would allow Australia to showcase its capability and international reputation in medical research, increase the number of clinical trials (particularly in areas of unmet need), and enable more powerful trials and analyses to be conducted. Facilities would include, for example:

- a secure online community and web portal for investigator-initiated trials
- collaboration facilities, including discussion groups, shared reviews, web-conferencing, and remote support for smaller institutions
- a portfolio of templates for trials design and analysis, data management techniques, etc.
- knowledge management facilities to define, evolve and promulgate standards and best practices for investigator-initiated trials, for example data monitoring and quality assurance
- online, classroom, blended and mobile learning facilities
- clinical data collection and management systems, optimised for investigator-initiated trials
- clinical data repository and data warehousing for trial analysis and reporting and meta-analyses

These facilities and infrastructure would be available to be shared with any sole investigator or collaborative group in Australia seeking assistance in conducting their own investigator-initiated clinical trial.

Education and career path for clinical trials research workforce

The current mix of professionals working in clinical trials research is diverse, including basic scientists, allied health professionals, psychosocial researchers and medical professionals.

There is a need to recognise:

- the specific education and training needs of these staff rather the ad hoc learning of the majority of trials researchers to date. Some existing programs cover ongoing

professional training modules, postgraduate qualifications (such as the Master of Clinical Trials); however, a more comprehensive program would benefit this group of professionals

- greater clarity in career paths
- relevant pay levels and position in organisations
- opportunities to work across different disciplines (secondments) to gain a broader understanding of the clinical research process, Resource sharing, for example, of researchers with (less common) specialist skills and experience
- formation of links to professional groups specific to clinical trials research.
- Funding of key trial coordinators directly from the health care delivery budget is needed (as in the UK through the NHS). Many hospitals rely on cross-subsidy from commercial studies to employ a research coordinator, but this creates tension between time available for 'paying' studies versus that available for network studies, even though the public health importance of the network studies is usually much greater than that of commercial studies.

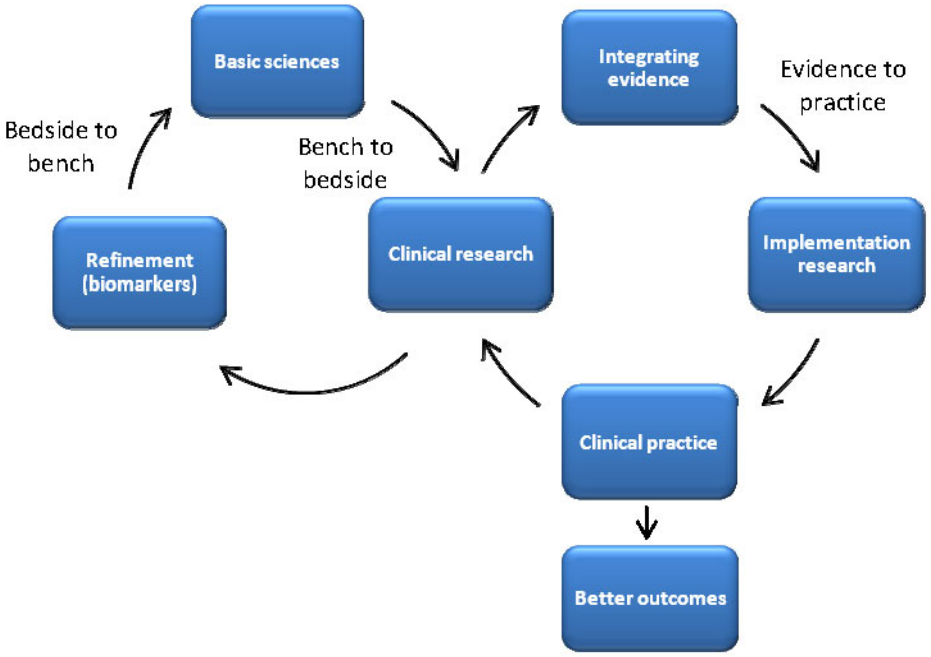
4. How can we optimise translation of health and medical research into better health and wellbeing?

It is critical that scientific and medical findings that benefit health and wellbeing are translated into standard clinical practice in Australia. Existing groups facilitate the translational of evidence in practice (see diagram below).

These groups need sustainable funding and infrastructure for their work.

We support the specific recommendations of the recent article by Scott and Glasziou in the *Medical Journal of Australia*.(13)

Translational research model



References

1. Department of Innovation Industry Science and Research. Australian Innovation System Report 2011. Canberra: Commonwealth of Australia;2011.
2. Khleif S, Doroshow J, Hait W. AACR-FDA-NCI Cancer Biomarkers Collaborative Consensus Report: advancing the use of biomarkers in cancer drug development. Clin Cancer Res 2010; 16: 3299-3318.
3. Khoury M, Gwinn M, Ioannidis J. The emergence of translational epidemiology: from scientific discovery to population health impact. Am J Epidemiol 2010; 172: 517-524.
4. Woolf S. The meaning of translational research and why it matters. JAMA 2008; 299: 211-213.
5. Califf R, Ginsburg G. Organizational Improvements to enhance modern clinical epidemiology. JAMA 2008; 300: 2300-2302.
6. Johnston S, Rotenberg J, Katrak S, Smith W, Elkins J. Effect of a US National Institutes of Health programme of clinical trials on public health and costs. Lancet 2006; 367(1319-27).
7. Clinical Trials Action Group. Clinically competitive: Boosting the business of clinical trials in Australia. Clinical Trials Action Group Report. Canberra: Commonwealth of Australia;2011.
8. Kenter M, Cohen A. Establishing risk of human experimentation with drugs: lessons from TGN1412. Lancet 2006; 368(9544): 1387-1391.
9. Roberts D, Dalziel S. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev 2006; (3): CD004454.
10. Evans J, van Wessem K, McDougall D, Lee K, Lyons T, Balogh Z. Epidemiology of traumatic deaths: comprehensive population-based assessment. World J Surg 2010; 34(1): 158-163.
11. Tarnow-Mordi W, Isaacs D, Dutta S. Adjunctive immunologic interventions in neonatal sepsis. Clin Perinatol 2010; 37(2): 481-499.
12. Tarnow-Mordi W, Hague W. Strategies to enhance recruitment to NHMRC multicentre clinical trials. Journal of Paediatrics and Child Health 2012: In press.
13. Scott I, Glasziou P. Improving the effectiveness of clinical medicine: the need for better science. Medical Journal of Australia 2012; 196(5): 304-308.

Appendix

The NHMRC Clinical Trials Centre (CTC) has a 20-year history in leading international clinical trials research with collaborating partners throughout Australia and overseas. Increasingly this research involves translating new discoveries and new ideas into better treatments and translating the evidence of clinical trials into better clinical practice and health policy. The CTC is well placed to lead important initiatives in the Translational Health Australia program and work with other key groups in new technologies: within NSW, across Australia and internationally.

Mission statement

The NHMRC CTC's mission is to achieve best practice in health care and improve outcomes in Australia and internationally through the better use of clinical trials research. Our goals are to:

- generate high quality evidence of the effectiveness of health care interventions through randomised trials
- be a national resource in design, conduct, analysis and interpretation of randomised trials
- improve evidence-based health care through the better use of clinical trials and high quality systematic reviews of trials

Research strengths of the NHMRC CTC

The NHMRC CTC has strong research capabilities in the following areas:

1. The Australian New Zealand Clinical Trials Registry (ANZCTR), the first national clinical trials registry, was established by the CTC and is managed and hosted here.
2. Expertise in biostatistics in the design and analysis of clinical trials
3. Expertise to oversee, monitor, review and provide advice on clinical trials research
4. Proven track record in clinical trial (investigator-initiated trials) design and coordination. Over the past 20 years, the NHMRC CTC has conducted 65 trials, recruiting 68,000 patients in therapeutic areas of cardiovascular disease, diabetes, neonatology and oncology.
5. Proven record of clinical trials changing clinical practice. For example, in the FIELD diabetes trial, fenofibrate, a lipid-modifying drug, reduced the risk of amputations in patients with type 2 diabetes and also reduced the need for laser therapy in patients with diabetic eye disease. In the SNAC trial, sentinel node biopsy for women with early breast cancer was shown to reduce arm swelling and to improve quality of life compared with traditional axillary clearance and is now incorporated into routine practice at major centres.
6. Capacity to personalise care based on new technologies (from bench to bedside). One example is the colorectal cancer trial, CO.17, in which a survival benefit of the molecular targeted agent, cetuximab was shown in patients with K-ras wild-type tumours. Patients with mutant K-ras tumours had no survival benefit. K-ras mutation

testing is now being routinely incorporated into clinical practice and will be included in future trials using therapies targeted at the EGFR receptor pathway

7. Expertise to incorporate health economic assessment into clinical trial design and the clinical research program
8. Expertise and capacity to evaluate trial evidence through systematic reviews
9. Expertise to guide clinical practice and health policy
10. Ability to assess low cost and effective treatment with large impact in Australia and internationally
11. Expertise to design and deliver postgraduate education including: Masters in Biostatistics (G08, group of eight Australian Universities); Masters in Clinical Trials (commenced in 2011), University of Sydney
12. Established national and international research collaborators
13. Expertise in developing economic modelling of cost of burden of disease and impacts on population of potential policy decision in health areas such as diabetes cardiovascular disease.

NHMRC CTC has strong research relationships internationally in the fields of diabetes, cardiovascular disease, neonatology and oncology and with national and international networks of such researchers.

The NHMRC CTC is the co-ordinating centre of clinical trials for 5 oncology collaborative groups (AGITG, ANZGOG, ANZUP, ALTG, COGNO) and performs randomisation service for the ANZBCTG. IT also has close links with the PC4 and ANZMTG collaborative groups.

The NHMRC CTC houses the collaborative group executive officers and staff for several of these groups and provides shared services.

The CTC also has many research links with international oncology collaborative groups.

In other therapeutic areas, NHMRC CTC also has strong research links with other international research groups including

- WHO
- VIGOUR
- Cholesterol Treatment Trialists Collaboration
- Cochrane Collaboration
- Prospective meta-analysis groups and trial collaborations in neonatology.