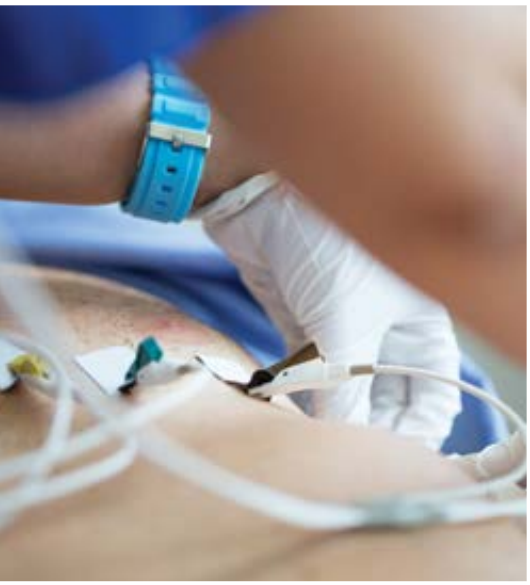
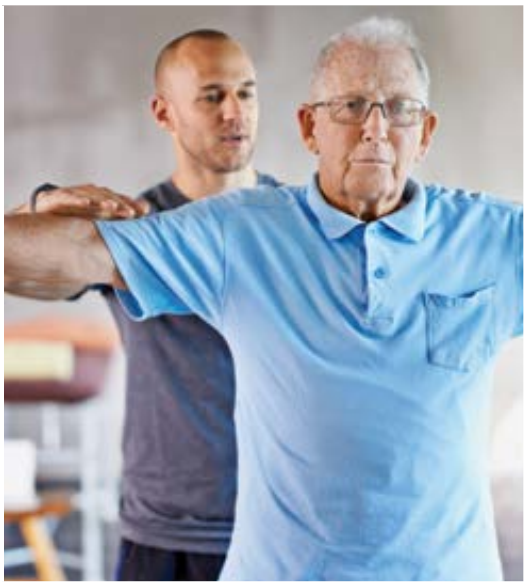
Australian Clinical Trials Alliance




Report on the Activities & Achievements of Clinical Trials Networks in Australia

2004 – 2014

Australian Government
National Health and Medical Research Council

This report was prepared by Australian Clinical Trials Alliance Ltd (ACN: 168 693 972)
for the National Health and Medical Research Council.

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Australian Government

Australian Clinical Trials

Participating Networks

Australasian College for Emergency Medicine Clinical Trials Group

Australasian Gastro-Intestinal Trials Group

Australasian Lung Cancer Trials Group

Australasian Radiopharmaceutical Trials Network

Australasian Sarcoma Study Group

Australasian Society for Infectious Diseases Clinical Research Network

Australasian Stroke Trials Network

Australia & New Zealand Breast Cancer Trials Group

Australia & New Zealand Melanoma Trials Group

Australia New Zealand Gynaecological Oncology Group

Australian & New Zealand Children's Haematology/Oncology Group

Australian & New Zealand College of Anaesthetists Clinical Trials Network

Australian & New Zealand Intensive Care Society Clinical Trials Group

Australian & New Zealand Urogenital & Prostate Cancer Trials Group

Australian Epilepsy Clinical Trials Network

Australian Musculoskeletal Clinical Trials Group

Australian Paediatric Research Network

Australian Primary Care Research Network

Cooperative Trials Group for Neuro-Oncology

Multiple Sclerosis Research Australia Clinical Trials Network

NSW Better Treatments 4 Kids

Paediatric Research in Emergency Departments International Collaborative

Paediatric Trials Network Australia

Palliative Care Clinical Studies Collaborative

Primary Care Collaborative Cancer Clinical Trial Group

Psycho-Oncology Co-operative Research Group

The Australasian Consortium of Centres for Clinical Cognitive Research

The Australasian Kidney Trials Network

The Australasian Sleep Trials Network

The Spinal Cord Injury Network

The Australian Type 1 Diabetes Clinical Research Network

The Interdisciplinary Maternal Perinatal Australasian Collaborative Trials Network

Therapeutic and Vaccine Research Program, Kirby Institute

Trans Tasman Radiation Oncology Group

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Executive Summary

Australia is regarded as a world leader in the design and conduct of high impact investigator-initiated clinical trials. Often referred to as 'public good trials', these studies are conducted in the absence of commercial interest and are designed to answer important clinical questions, providing unbiased scientific evidence to help consumers, clinicians and policymakers make decisions about which treatments, tests and services are most effective or offer the best value for the healthcare system.

Generating the level of evidence needed to reliably inform clinical practice or healthcare policy requires large collaborative clinical trials that are conducted across multiple centres and involve many hundreds or thousands of participants, healthcare practitioners and researchers. In Australia, and throughout the world, clinical trials networks (sometimes referred to as clinical trials groups or collaborative trials groups) have been formed as a means of bringing together a large community of clinical researchers with a common interest in advancing the evidence base for a particular area of clinical practice. These multidisciplinary collaborations result in horizontal and virtual networks of clinical research leadership, expertise and capacity that are integrated within the healthcare system.

Over the last 25 years, the number of clinical trials networks within Australia has steadily grown, along with the recognition that networks are a vital component of both a high-quality healthcare system and a strong and competitive clinical trials enterprise in Australia (which includes commercial and public good trials). However, our understanding of this unique component of our clinical trials sector – in terms of what networks exist, how they are formed and sustained, and the scope and impact of their research – and how best to support and enhance the vital work undertaken by clinical trials networks, has been limited. In 2014, the National Health and Medical Research Council commissioned the Australian Clinical Trials Alliance to report on the activities and achievements of Australia's clinical trials networks over the last decade. A comprehensive survey of national or state/jurisdiction-based clinical trials networks was undertaken with the aim of describing the structure and core functions of networks and capturing a detailed snapshot of studies completed and published, or currently being conducted, by networks within the last 10 years.

There were 37 clinical trials networks identified in Australia of which 34 contributed data for this report. These networks span a wide range of clinical disciplines and disease groups and incorporate upwards of 10,000 clinical researchers across the country – the majority of whom are practicing clinicians. Whilst the formation of most networks was driven from within a clinical community, these groups uniquely bring together clinical experience with a broad range of expertise in trial design and conduct, including research coordination, project management, data management and biostatistics. There were networks actively researching across all levels of the healthcare system – including acute, sub-acute and primary care or community settings and, importantly, the majority undertake trials in sites throughout rural and regional Australia as well as the major metropolitan centres.

There was a wide range of activities reported to be 'core functions' undertaken by the networks surveyed, but common among almost all networks was a key role in supporting the collaborative development of research proposals and a process of internal peer review of study proposals and protocols to ensure scientific merit and rigour. Despite the size of their membership and the scope and significance of their research within the health system, networks by and large have relatively low levels of central infrastructure, which, in part contributed to the incompleteness of data used in this report.

Collectively, the clinical trials networks participating in this study have published in the last 10 years, or are currently undertaking, more than 1,000 studies that involve (or will involve at completion) close to one million participants. The vast majority of these studies were phase II, III or IV clinical trials and whilst many involve multinational collaboration, more than half were designed and led by Australian investigators. The total estimated amount of research funding reported for these studies was more than $1 billion, which included public and private funding generated from within Australia and overseas.

Australian clinical trials networks have made a substantial contribution to the global evidence base across an array of different conditions. More than 100 high-profile studies that have directly influenced clinical practice and/or healthcare policy – both within Australia and internationally - were reported. Networks have also been highly successful at forging partnerships with investigators overseas to conduct multinational clinical trials, and these relationships are particular strong with Canada, the United Kingdom, the United States and France.

Whilst this report suggests that a substantial proportion of Australia's clinical research effort has come from clinical trial networks over the past decade, it is likely that these figures are a significant underestimate of true activity. This is due to major limitations in the amount of data that networks were able to provide (largely attributable to limited resources) or that could be sourced from public records. For some figures, this could be as much as half of the total amount reported. Furthermore, where studies involved international collaboration, the portion of total recruitment and total funding that arose from within Australia could not be determined.

Major data limitations were also encountered when attempting to accurately determine the relative proportion of clinical trials networks activity to total clinical trial activity in Australia. A conservative estimate is that over the last 10 years, network trials have received at least one third of all funding awarded by the National Health and Medical Research Council for clinical trial-related activity during this period, and around half of the funding awarded for grants for clinical trials with budgets that exceeded $1 million.

Data from the Australian and New Zealand Clinical Trials Registry and ClinicalTrials.gov indicated that networks may have undertaken at least one quarter of the large non-industry trials (trials with a target sample size of more than 1,000 participants) conducted in Australia in the last decade. However, this could not be accurately determined and this finding supports the well-recognised need to develop mechanisms that facilitate collection and reporting of accurate data of clinical trials activity in Australia. This applies particularly in relation to investigator-initiated trials where both public investment and participation in these trials is considered an essential underlying component of our healthcare system.

This landmark report provides a unique and valuable snapshot of the activities and achievements of clinical trials networks in Australia. It highlights that clinical trials networks have made an immense contribution to the clinical evidence base across numerous clinical disciplines. However, it also points to the fact that there are high disease-burden areas of the health system that do not have a nationally coordinated clinical trials network currently. It is also likely that existing networks would achieve substantially more for the public good if they had access to better infrastructure and additional funding. It is hoped that this report will serve as a basis to inform future research, policy development and investment to maximise the capacity of Australian clinical trials networks, and a benchmark against which to evaluate the future impact of these efforts.

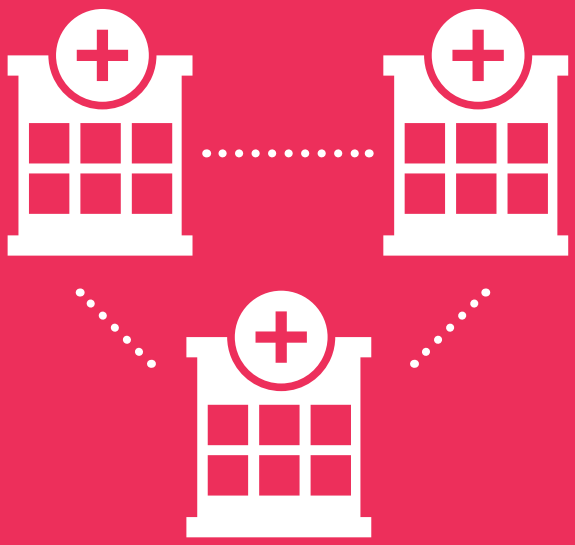
Key Facts AT A GLANCE

COLLECTIVELY

34 clinical trials networks that participated in this study represent more than

10,000

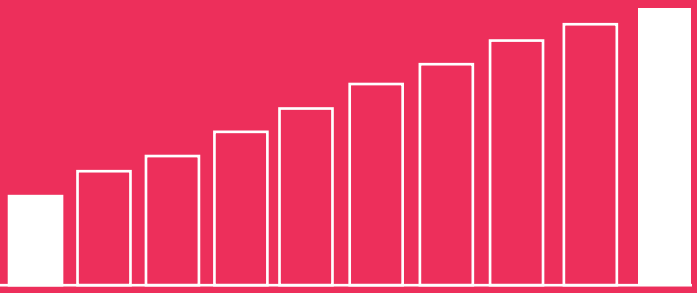
HEALTHCARE PRACTITIONERS AND RESEARCHERS.



Networks undertake a range of different activities but have the common core function of enabling the collaborative development and internal peer-review of research proposals.

Networks are extensively integrated with acute and sub-acute hospitals as well as primary and community care facilities across all jurisdictions and into regional and rural areas of Australia.

The total number of studies published by networks per year appears to have more than doubled between 2004 and 2014.

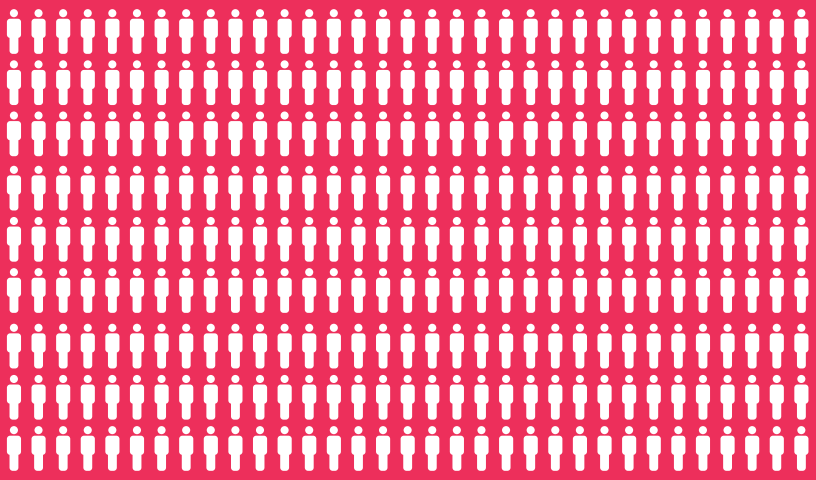


Australian clinical trials networks have together completed and published or initiated more than

1,000 STUDIES

IN THE LAST DECADE, REPRESENTING MORE THAN

1 MILLION PARTICIPANTS



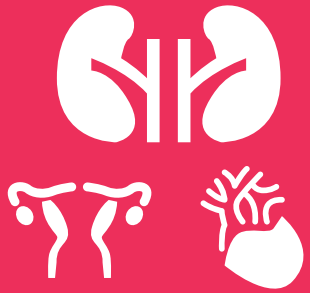
AND AT LEAST

$1 BILLION

IN TOTAL RESEARCH FUNDING

(possibly much more)

Networks have been established across a wide range of clinical disciplines and disease groups, but there are still areas of high disease-burden that don't have a nationally coordinated clinical trials network, such as heart disease, mental health and asthma.



Key Facts AT A GLANCE

Networks have variable (and predominantly limited) capacity to report their aggregated research inputs and outputs or to report recruitment in near real-time. This may be attributed to the fact that these networks have relatively low levels of central infrastructure and employ a median of only 1.9 FTE per network.

- ☑ **Change Practice**
- ☑ **Change Policy**

THERE ARE MORE THAN

100 EXAMPLES

Of prominent clinical trials published by networks in the lastdecade that have had, or are expected to have, a direct impact on clinical practice and policy.

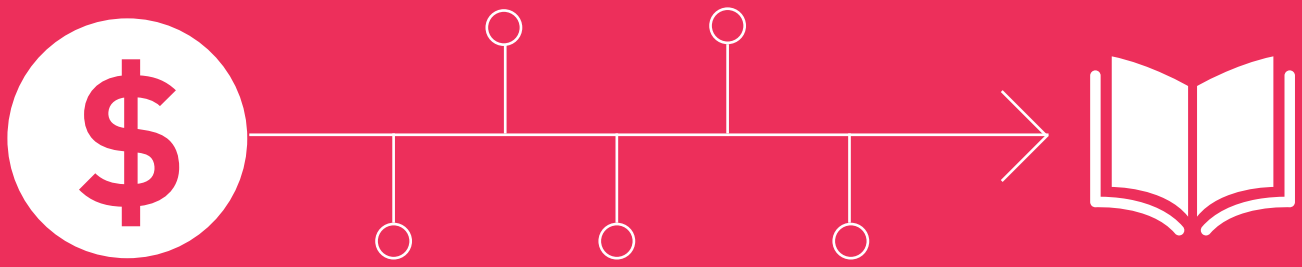
Networks have developed extensive global partnerships to undertake multinational trials, but more than half of their studies are deigned and led by Australian investigators.

It is currently impossible to accurately determine the proportion of clinical trial activity within networks to total clinical trial activity in Australia. A conservative estimate is that networks undertake approximately 7-19% of all non-industry clinical trials, and

ONE QUARTER OF LARGE NON-INDUSTRY CLINICAL TRIALS WITH A SAMPLE SIZE >1,000 PARTICIPANTS CONDUCTED IN AUSTRALIA

The median interval between the date of first funding of a network trial by the NHMRC and publication of the primary results

IS ONLY 5 YEARS.



It is currently impossible to accurately determine the proportion of NHMRC funding for clinical trials that has been received by networks. A conservative estimated is that studies undertaken by networks account for approximately one third of all NHMRC funding awarded for clinical trial-related activities since 2000, and

APPROXIMATELY HALF OF THE FUNDING AWARDED FOR LARGE CLINICAL TRIALS WITH BUDGETS GREATER THAN $1 MILLION.

1

Introduction

1 Introduction

1.1 Background

1.1.1 Clinical trials

Clinical trials enable the testing of hypotheses that are concerned with evaluating the effectiveness, efficacy or cost-effectiveness of a biomedical intervention (including preventive measures, treatments, clinical strategies, and diagnostic tests) in patients. They are a fundamental component of the process of generating evidence to inform clinicians, health consumers, and policymakers about the most effective and cost-effective ways of preventing, diagnosing and treating ill health and improving health outcomes. Clinical trials are an essential link in the chain of translation and also drive innovation. In general, the evidence obtained from randomised clinical trials defines international best practice for the treatment of any disease, health condition or clinical discipline. Hence they form the basis of international or national clinical guidelines that inform state of the art, high-quality healthcare.

Novel treatments are usually developed through a process that exploits fundamental knowledge of a biological mechanism to develop a new intervention that is be expected to result in a health benefit. However, the experience of decades of clinical research is that some such interventions are ultimately proven - via well-conducted randomised clinical trials - to be either ineffective or actually harmful. These trials use well-established scientific methods that are necessary to achieve validity and reliability for a given result, but they are not foremost an 'academic' exercise. Rather, clinical trials are a practical and pragmatic means of providing reliable information that for individuals, helps save and improve lives, and for society, helps to inform the most valuable use of scare health resources.

1.1.2 Who conducts clinical trials?

Although there can be some overlap, clinical trials are broadly categorised into those conducted by two groups: Commercial entities such as pharmaceutical companies or clinical research organisations; and clinical investigators working within the healthcare system or based within a public academic institution such as a university. These are hereafter referred to as commercial clinical trials and investigator-initiated clinical trials:

Commercial trials are conducted by organisations that typically own or have a financial interest in the intellectual property related to the intervention being tested. Commercial organisations use the information obtained from the trial for many reasons including to support regulatory applications to obtain licenses to sell their products, to support applications for private or public subsidy of the cost of providing the product, and to support marketing the product to clinicians, patients, and Governments.

Trials that are conducted to support regulatory applications are often designed in conjunction with regulatory agencies such as the United States Food and Drug Administration (FDA) or the European Medicines Agency (EMEA). These trials provide valuable evidence to support the licencing of new products or procedures, but they do not always provide answers to all of the questions that are relevant to the introduction of the new intervention into clinical practice. This may be because the commercial trial was conducted in a highly specific population and clinicians are left uncertain about whether the results can be extrapolated to other groups of patients, the trial evaluated the intervention under ideal rather than

routine or 'real-world' circumstances or because the comparator group may not be relevant to usual clinical practice.

Investigator-Initiated Clinical Trials are trials that are conceived and conducted by independent clinicians and academic researchers. These trials serve the broad purpose of generating clinical evidence to improve health care (where that evidence does not exist) rather than for a commercial imperative.

1.1.3 What are investigator-initiated clinical trials?

Investigator-initiated clinical trials provide a public good. These are trials that address clinically relevant research questions that are important to clinicians, patients and policymakers. They advance the public good because they seek to identify the best intervention, irrespective of its commercial relevance. Examples of investigator-initiated trials include the evaluation of:

- licensed products to replicate the results of commercially conducted trials;
- licensed products but within a pragmatic design that tests the effectiveness of the product as used in routine clinical practice rather than in tightly controlled circumstances;
- licensed products in patient groups that extend beyond those used in commercial trials to establish additional areas in which a product may be helpful (off-label trials);
- new uses for old drugs that are no longer on patent;
- two or more types of standard care, irrespective of whether standard care involves a licensed product (comparative effectiveness research);
- clinical algorithms or protocols that combine multiple components related to diagnosis and treatment or both (process-of-care trials and systems-of-care trials); and
- non-drug and non-device biomedical interventions.

1.1.4 Benefits of investigator-initiated trials

Investigator-initiated trials have often been used to demonstrate, that widely adopted components of standard care for many diseases were either ineffective or harmful. An example of an advance in medical care that arose from investigator-initiated public good trials was the discovery that aspirin, a drug that was almost 100 years old, was highly effective at reducing death in patients with an acute myocardial infarction(1).

Some investigator-initiated trials will also have commercial relevance because they evaluate some aspect of a commercially provided intervention. However, investigator-initiated trials are conducted by investigators who are conducting trials independent of any commercial organisation or the commercial relevance of study outcomes.

The extent to which clinicians can call upon evidence derived from well-conducted clinical trials to guide their practice varies substantially between disciplines. The dramatic improvement in survival that has occurred in many forms of childhood cancer, particularly leukaemia, is a consequence of embedding trials within routine clinical practice so that new chemotherapy regimens were serially tested against best known current treatments resulting in massive iterative improvements in outcome (2). However, there are many other disciplines of medicine, including anaesthesia, intensive care, infectious diseases, neonatal medicine, nursing, physiotherapy, and surgery, where only a small proportion of clinical decision making can be guided by evidence derived from well conducted clinical trials. Where there is insufficient evidence,

patients and policymakers are left uncertain as to the most effective and cost-effective interventions and this paucity of evidence often promotes unwarranted variation in clinical care (3). Investigator-initiated trials play a vital role in enhancing the evidence base, particularly when there is no commercial imperative for the evidence to be generated.

1.1.5 Clinical trials networks

Whilst clinical trials are just tools in the development of a self-improving health system, they are nonetheless complex and require considerable methodological expertise (such as in statistics, epidemiology, and data management) and training. They may also require a large number of patients to participate in a clinical study in order to identify relatively small but significant health gains. Hence most investigator-initiated clinical trials are conducted by groups of clinicians in collaboration with the appropriate experts. The involvement of clinicians serves to maximise the likelihood that the questions being prioritised are those that are most relevant to improving clinical practice.

A clinical trials network, also known as clinical trials group or a collaborative trials group, is an organised group of clinicians and other researchers who share infrastructure that enables them to collaborate to conduct multiple multicentre clinical trials. Clinical trial networks exist throughout the world and their number is increasing progressively. These networks are both horizontal and virtual in that they involve researchers and sites that conduct trials that are geographically dispersed. Some networks are restricted to a city or a state, others are national or international, some are global, but all involve multiple healthcare centres and are virtual in that they don't require buildings, laboratories or equipment used in areas of basic research. In many diseases and clinical disciplines, these networks of clinicians have formed close collaborations with people with relevant methodological expertise order to efficiently conduct and coordinate both small and large clinical trials.

Clinical trials networks have the potential to create innumerable synergistic interactions - that is, their sum is substantially more than their constituent parts. The constituent parts are: the sites that enrol patients into trials; investigators that plan, conduct, analyse, and report trials; and central trial coordination and data management. Synergies of efficiency that facilitate the conduct and quality of trials conducted by networks include:

- The network is a community of clinicians and other researchers. The community has a shared sense of challenge and achievement associated with the conduct of trials. The individuals who provide leadership for a network are responsible to, and representative of, their community, which has a shared mission and vision to generate high quality evidence that improves patient care in a particular discipline or field of medicine.
- Networks provide the capacity to generate trials with larger sample sizes. Many trials need to recruit thousands of patients to have sufficient statistical power to demonstrate small but highly clinically relevant effect sizes. Networks provide a larger number of sites, working together on the same study, addressing the same question because of its clinical importance and in this manner, often facilitate greater recruitment that non-network trials.
- Networks have the capacity to conduct multiple sequential trials, with new trials starting as old trials complete, sometimes informed by the results of the earlier study. This means that research coordinators (or research nurses) who recruit patients, help deliver interventions, and collect data at individual sites, can be employed across multiple projects. Similarly research staff employed within the networks can be retained to more efficiently move from one project to the next. This lowers the marginal cost of conducting trials but also ensures that experienced research personnel

do not need to be recruited and trained for each new trial. It is this collective workforce of clinical research personnel at the level of sites and within clinical trials networks that forms part of the essential infrastructure required for this type of research.

- Networks are horizontally devolved with the only requirement for sites to participate being that they treat or see patients who are suitable for inclusion in the networks' trials. As such, networks tend to have sites in non-teaching as well as academic institutions, and have sites in rural and regional locations as well as metropolitan locations. This also allows the evaluation of interventions across the full range of locations in which the results would be implemented into actual clinical practice. This feature substantially enhances the external validity of trials – that is, the results of trials are more likely to apply to all patients than just patients seen in tertiary centres.
- Networks have shared intellectual infrastructure; the knowledge and expertise associated with the design, conduct, analysis, and reporting of clinical trials is shared among all the investigators in the network. Networks often undertake extensive internal peer-review of trial plans and manuscripts before these are submitted for funding applications and publication, respectively. This allows the networks to maximise the validity, feasibility, and impact of the trials that they conduct and also ensures a greater chance of funding due to the quality of the study design.
- Networks often own or utilise shared infrastructure that is necessary for the central management of trials including project management, data management, and appropriate statistical analysis. They also can facilitate the development of standardised study tools, for example, the definitions of variables used for entry criteria and evaluation of outcome, which promotes comparability across studies.
- The network infrastructure, once created, is preserved for future trials. Stand-alone trials, conducted outside a network, must recreate the infrastructure for each new trial. This allows networks to conduct more trials and recruit more participants per dollar of public funding.
- Over time, networks develop a brand that arises as a consequence of the shared track record of the network. This 'brand value' gives confidence to journal editors, funding bodies, and guideline developers about the quality of trials conducted by the network. Networks are highly invested in ensuring the success and quality of all projects because their brand value is dependent on creating and maintaining the highest possible standards. Such 'branding' is almost certainly likely to lead to increased international collaborations which not only allows clinically important questions to be addressed more quickly, but also brings novel ideas and products not otherwise available to Australians through the clinical trials networks.
- Although it has never been evaluated empirically, it is highly likely that the results of trials conducted by networks are translated more rapidly into clinical practice. This 'in-built' translation arises as a consequence of the participation of a diverse and extensive group of clinicians in the design and conduct of the trial. Having done the trial, they are more likely to believe the findings and thus become highly incentivised to implement its findings into their own clinical practice.
- While clinical trial networks are independent of industry, this does not preclude their collaboration with industry. Where the interests of both a network's researchers and a commercial entity are aligned, this allows sharing of resources, expertise, and infrastructure to conduct trials.
- Clinical trials networks generally establish an array of relationships that greatly enhance their effectiveness and efficiency. These key partnerships include relationships with academic organisations, such as Universities and Medical Research institutes (MRI), Colleges that undertake training of medical specialists, special Societies that represent the interests of clinicians as well as consumer and advocacy groups associated with specific conditions. This spectrum of relationships vastly enhances the effectiveness and impact of the work conducted by networks.

1.2 The value of clinical trials networks

1.2.1 The funding & policy landscape for clinical trials in Australia

Clinical trials are expensive. Many of the highest value Project Grants that are awarded by the National Health and Medical Research Council (NHMRC) are used to conduct investigator-initiated clinical trials. The resources utilised by networks to conduct trials can be divided into resources that support the central infrastructure of the network and the resources that are used to conduct specific clinical trial projects. In turn, the resources used to conduct specific clinical trials projects can be further divided into those that support the central project coordination and those that support the direct costs of participant recruitment, delivery of an intervention, and collection of data at the site or practice level.

The central infrastructure of the network represents the component that supports the collaborative development of trials but not expenditure on direct trial conduct. Network activity involves both paid staff and volunteers. However, most paid staff involved in network activities are not employees of the network but rather are employed by Universities or MRIs (predominantly to undertake central trial coordination), or by hospitals (for example, to recruit participants, deliver interventions, and collect data). As such, networks often have a range of key partnerships with Universities, MRIs and hospitals, as well as Clinical Societies and Colleges, some of which host and support networks. The role of volunteers, and the goodwill of both volunteers as well as paid staff, cannot be underestimated as a critically important resource that is harnessed by networks to facilitate their work.

1.2.2 Why this report is timely and important

There are a number of initiatives at various levels of Government that in some way aim to improve the research capacity of investigator-initiated clinical trials networks: either through direct central infrastructure support for networks; access to platform technologies; improving the efficiency of trial processes including those related to ethical and governance regulation; better funding models for clinical trials; and enhancing collaboration and coordination between networks.

Despite the importance of networks in generating high-quality evidence to inform practice and policy, and the fact that clinicians participating in the work of these networks do so on a daily basis as part of their routine clinical roles in order to improve healthcare outcomes, relatively little is known about the composition, size, activity, impact, and sustainability of the investigator-initiated clinical trials sector in Australia. There is limited understanding about how Australian networks have been formed, developed, structured and sustained; the volume and type of trials completed and underway; the major outputs of networks; how many clinicians and researchers are engaged; and where clinical trials expertise does and doesn't exist across disease and discipline groups. Similarly, the proportion of investigator-initiated clinical trials that are addressing health issues for specific patient populations within Australia and the level of cross-discipline or international collaboration that exists are not known.

A better understanding of clinical trials network activities will be an invaluable resource to inform key stakeholders about clinical trial capacity, identify where new networks could be supported, drive decision making to enhance the sector, and serve as a benchmark against which the impact of initiatives to enhance the sector can be evaluated.


164
35.0
710
4.47
0.00
0.00
0.00
1.18

2 Aims

3 Methodology

2 Aims

This report presents the results of a study referred to herein as the 'Profiling Networks Project'. The study was developed in consultation with and support from the NHMRC as part of the Australian Government's commitment to expediting clinical trials reform. The aim of the project was to develop a better understanding of clinical trials networks in Australia –how networks are formed, structured and sustained, and to provide information about the research activity that they undertake and the contribution these networks have made to the health system.

The information collected included details of the networks' membership, geographical reach, funding (both central network funding and research project funding), research focus (including whether trials are addressing health issues in Indigenous and vulnerable populations), the number and type of trials completed and underway, number of patients recruited to trials, proportion of investigator-initiated compared to commercial trials, research outputs and impact and major collaborators.

The Australian Clinical Trials Alliance (ACTA) was engaged by the NHMRC in June 2014 to produce a report on existing clinical trials networks in Australia including:

- Information on the relative contribution of clinical trial networks to clinical trials activity in Australia;
- An analysis of literature and reference material to determine whether networks have had a tangible effect on the health of Australians and on the health system;
- An analysis of the current models of establishing and maintaining networks, including interactions and interdependencies; and
- Advice on how to measure 'point in time' data on all currently recruiting clinical trials in Australia.

3 Methodology

3.1 Project governance and management

A steering committee comprising senior representatives from several networks, NHMRC and ACTA was established to oversee a national survey to collect data for the report (see appendices 4.1). A project team based at ACTA undertook direct management of the Profiling Networks Project. The project team was led by Rhiannon Tate (Executive Officer, ACTA) and included Anne Woollett (Senior Project Officer), Carly Smith (Project Officer), Anastasia Ossoukhova (Project Officer), Nazmul Karim (Biostatistician) and Dinesh Giritharin (Research Student). The study (Project No: 410/10) was considered for Low Risk Review and received approval from the Alfred Health Human Research Ethics Committee on 22 September 2014.

3.2 Identification of clinical trials networks

Among the clinical research community there is some debate as to how to define an investigator-initiated clinical trial network since any investigator-initiated trial involving multiple sites requires a network of like-minded investigators for its success. As part of ACTA's ongoing work to build a membership of clinical trials networks across the sector, an early working definition of a network was discussed at the 2013 National Summit of clinical trials networks and received broad *in principle* support. In the absence of any nationally agreed definition, the ACTA working definition of a network was used as the first step in identifying participants for the Profiling Networks Project (see **Box 1**) although the requirement for a network to have completed and published at least one study was not applied for this project.

Several methods were used to identify networks for inclusion in the study. The index of clinical trials networks compiled previously by the NHMRC and published on the *australianclinicaltrials.gov.au* website was used as the starting point for identifying networks. This list was developed in order to address Recommendation I of the 2011 report of the Clinical Trials Action Group to 'facilitate better national coordination and greater collaboration across clinical trials networks" (4). In August 2013, there were 149 organisations listed in this index. This list, and the associated description of organisations, was used to identify groups that were likely to meet the working definition of a network.

Thirty-six groups were initially identified as potentially meeting the definition of a clinical trials network. The remaining organisations were identified as MRIs (n=42), Peak/Consumer Bodies (n=14), Trial Registers/Databases/Recruitment Tools or Services (n=12), Academic Trial Coordinating Centres/Contract Research Organisations CRO) (n=11), Charitable Organisations/Research Funding Bodies (n=7), Clinical Trials Units (n=6), Professional Bodies (n=4), Commercial CROs (n=3), Government/Statutory Bodies (n=3), Clinical Services (n=2), Clinical Registries (n=1) and Consultants/ Other Research Partnerships (n=7).

The NHMRC Funding Dataset (2004-2013) was then interrogated to identify project grants awarded for clinical trials in the 10 years to 2013, which was the most recently available data at that time. Of the 6181 project grants awarded, 1827 were identified within the Broad Research Area "Clinical Medicine and Science". A basic word search for "Trial" in the Scientific Title, Simplified Title, Research and Health Keywords yielded 323 relevant grants for the period *(excluded 6 x "atrial" + 1 other non-clinical trial).* The names of the grant-holders and the Principle Investigators were used to manually web search for any

additional networks but this did not identify any further networks. One previously unidentified network contacted ACTA during the course of the study and was invited to participate.

Box 1. ACTA working definition of an investigator-initiated clinical trials network

Investigator-initiated clinical trials networks are national or state-based networks or groups of clinician researchers that:

- are active in a defined area of clinical trials research
- have agreed and documented governance processes for collaborative development, conduct and publication of investigator-initiated, multicentre trials
- have conducted or are conducting multicentre, investigator-initiated clinical trials and whose members have completed and published at least one study in a peer reviewed journal
- demonstrate an ongoing commitment to work collaboratively and conduct further trials to improve the evidence base for high-quality healthcare.

3.3 Collection of information from networks

Data were obtained from Networks between November 2014 and April 2015 using an online survey tool (Survey Monkey) that requested information about the network, and a Microsoft Excel template was used to collect information about networks' research activities and achievements. A copy of the online survey tool can be viewed online (http://bit.ly/1OmNe9r).

The on-line survey comprised 50 questions categorised into 5 areas:

- Network demographics and administration
- Network membership
- Network infrastructure
- Participant recruitment
- Major achievements of the network

Additional information was collected from each network, using an Excel template, for all studies being conducted currently or completed (main results published) by the network between 2004 and 2014. A blank copy of the Excel template can be viewed online (http://bit.ly/1PNuTBO).

Ongoing studies were sub-categorised as: funded and in development but not yet recruiting; open for recruitment; recruitment completed and in follow-up; completed with the primary manuscript under development; completed with the primary manuscript submitted for publication; or terminated without being completed. The information that was sought for each study included:

- Study name/acronym
- Trial registration number
- Study type

- Study initiator
- Study sponsor
- Current progress status
- Sample size (actual for completed studies and planned for current studies)
- Approximate total funding and primary/other funding sources
- Year first funded (for unpublished studies)
- Year main results published (for completed studies)
- NHMRC grant identifier (where applicable)
- Collaborators (national and international)
- Primary results citation + other publications arising from the study
- Impact of the study on clinical practice or policy or both

The survey tool underwent an initial round of pilot testing by three networks and was modified subsequently based on the feedback that was received. A second round of testing was conducted by one of the original pilot groups.

In the first instance, networks were asked to complete the online survey and provide data related to their studies using the Excel template (self-report). If networks were not able to provide information, for example, because of insufficient staffing resources to provide comprehensive data on their research activity or because they did not have the data accessible in a central repository, assistance was offered by the project team to complete the Excel template.

Where members of the ACTA project team were responsible for collecting and collating information, publicly available sources were used to compile the most complete dataset possible. These sources included information extracted from the network's website, newsletters and annual reports, and those of any international collaborators; clinical trial registries (e.g. Australian and New Zealand Clinical Trials Registry (ANZCTR), ClinicalTrials.gov (CT.gov), World Health Organisation International Clinical Trials Registry Platform); the NHMRC research funding datasets; publications of study results; and general web searches. Excel templates completed by the project team were then returned to the networks for validation and resolution of queries. In particular, networks were encouraged to provide information about the impact of their studies on clinical practice and policy as the project team could not readily obtain this information form publically available sources.

3.4 Data from the NHMRC

The NHMRC's Clinical Trials 2000-2014 funding dataset was provided by the NHMRC in April 2015 to facilitate a comparison of funding awarded to networks for clinical trials compared with clinical trials conducted by investigators not associated with a clinical trials network. A process map outlining the steps undertaken to identify grants awarded to networks is provided in Appendix C. Further notes on interpreting the results of this analysis are provided in the relevant section of the report.

3.5 Data from the ANZCTR and CT.gov

Data custodians of the ANZCTR provided two separate datasets to support an analysis of trial activity undertaken by networks compared with all other trial activity in Australia. One dataset contained information extracted from the registry for all interventional studies with at least one participating site that was located in Australia that were registered between 2005 (when the ANZCTR commenced) through until 31 December, 2014. The second contained information extracted using the same search parameters at ClinicalTrials.gov (CT.gov.) Staff at the ANZCTR identified duplicate studies (i.e. those that appeared on both registries) and the project team, using a limited number of variables that could be readily matched between the ANZCTR/CT.gov, constructed a combined dataset of unique studies. These included the anticipated start date of the trial (i.e. the date the first patient was expected to be enrolled into the trial), trial type or phase, sample size, type of trial sponsor (classified as either industry or non-industry) and the primary field of research code or Medical Subject Headings (MeSH) code. A process map outlining the steps undertaken to identify clinical trials conducted by networks (phase I-IV trials or pilot/feasibility studies) among those registered on the ANZCTR/CT.gov is provided in Appendix D. Further notes on interpreting the results of this analysis are provided in the relevant section of the report.

3.6 Data management and statistical analysis

Information obtained was cleaned and coded by the project team and entered into SPSS. Data management was performed in four distinct steps:

Analysis of "ACTA National Survey of Clinical Trials Networks 2014" responses
The dataset retrieved from the online survey responses were entered into an SPSS template. Descriptive statistics of network level data and aggregates were generated. Frequency and relative frequency were generated; bar charts, panel bar charts and pie charts were used to illustrate summary statistics in terms of number of networks. Complete case analysis was conducted leaving missing information dropped. Bar charts were generated to illustrate descriptive statistics, in terms of number of network.

Analysis of "Question 34A and 34B" spread sheet
Excel spread sheets received from each of the networks included information on current and published studies. These spread sheets contained responses describing details of network research activities, outputs and impact on clinical practice and healthcare policy. Data were screened for discrepancies and cleaned accordingly. Missing data were treated as incomplete and complete case analysis was performed. Duplicate studies were identified and excluded from the analysis. Descriptive statistics were generated. Summary statistics for numerical data such as total funding and sample size were generated. Where necessary, network aggregate figures were generated across groups and displayed using bar charts. To facilitated comparison cross tabulation of variables was undertaken and results were illustrated by bar charts and panels.

Analysis of network clinical trials activity against NHMRC dataset
The relative contribution of clinical trials identified as being conducted by a network compared to all trial activity in Australia was explored through linking of the ACTA clinical trial dataset (from Q34 of the survey) with NHMRC Clinical Trials 2000 – 2014 data set and subsequent comparative analysis. Results were displayed through bar and line graphs. The NHMRC Clinical Trials 2000–2014 data analysis process map is presented in Appendix C.

Analysis of network clinical trials activity against ANZCTR dataset

Examination of clinical trials registered on the ANZCTR or CT.gov was done through linking of the ACTA clinical trial dataset (from Q34 of the survey) with the ANZCTR clinical trials dataset. Comparative analysis was performed. Results were displayed through bar and line graphs. The ANZCTR/CT.gov data analysis process map is presented in Appendix D.

4

Clinical Trials Networks in Australia

4 Clinical Trials Networks in Australia

4.1 What networks exist in Australia?

A total of 37 investigator-led clinical trials networks were approached to be included in the report. Of these 34 networks (92% response rate) agreed to participate and provided information or consent for information to be abstracted from publically available sources or both. Two of the participating networks only partially completed the online survey component of the study but provided consent for data related to their current and published studies to be included in the report.

The number of networks that provided a response for each of the survey fields is reported in association with the results as they are presented. Networks were offered assistance from project staff to complete the spreadsheet component of the survey related to current and completed studies (Question 34). In all, 14 participating networks provided comprehensive information about current and published studies, 17 networks required partial or complete assistance filling in this component of the survey, and 3 networks did not yet have reportable information.

The names of participating networks, together with their acronym, primary research focus, and the year in which they were founded are listed in Table 4-1**.** The first network established was the Australian and New Zealand Breast Cancer Trials Group, which was founded in 1979. Most networks were established relatively recently with 23 networks established during the last 10 years (2004-2014). The median and interquartile range (IQR) age of networks is 8.5 (8 - 14) years. Just over half of the participating networks (n=19) reported a primary area of research that was classified as being disease-based (e.g. cancer, stroke, kidney disease, epilepsy), with the remaining classified as discipline-based networks (e.g. primary care, intensive care, anaesthesia, paediatric emergency medicine). Overall, 12 networks had a primary focus related to cancer.

Networks were asked to identify whether specific subgroups of patients were a particular focus of the network's research. Neonates were identified by two networks, paediatrics by 11 networks, youth/adolescents by eight networks, older adults by 14 networks, Indigenous Australians by two networks, women by two networks, and patients with mental illness by three networks.

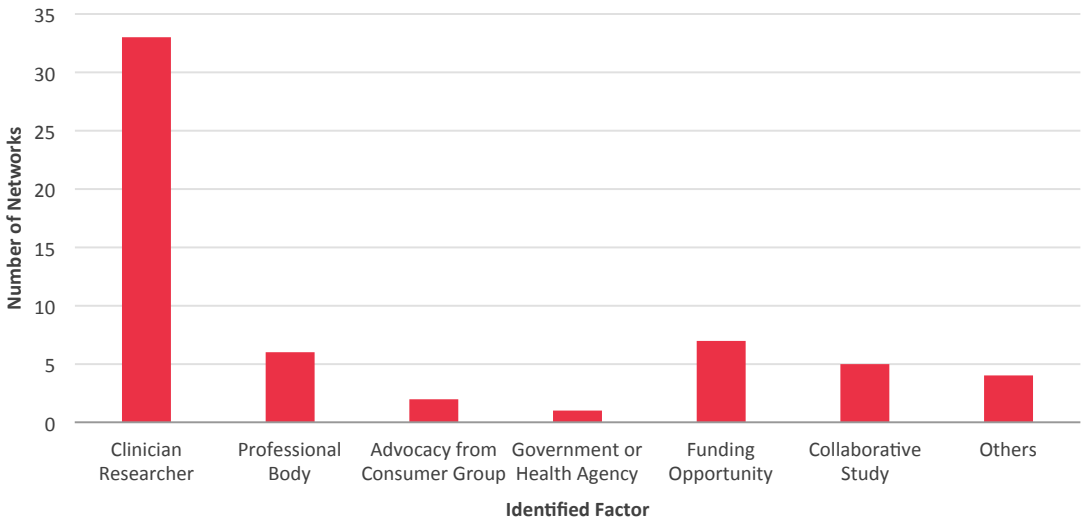
TABLE 4-1 PARTICIPATING CLINICAL TRIALS NETWORKS

	Network	Acronym	Primary Research Focus	Founded
1	Australia & New Zealand Breast Cancer Trials Group	ANZBCTG	Breast Cancer	1979
2	Australian & New Zealand Children's Haematology/Oncology Group	ANZCHOG	Paediatric Oncology	1986
3	Trans Tasman Radiation Oncology Group	TROG	Radiation Therapy Treatments & Techniques	1989
4	Australasian Gastro-Intestinal Trials Group	AGITG	Gastro-Intestinal Cancer	1991
5	Australian & New Zealand Intensive Care Society Clinical Trials Group	ANZICS CTG	Critical Care Research	1994
6	Interdisciplinary Maternal Perinatal Australasian Collaborative Trials Network	IMPACT	Maternal/Perinatal Medicine & Health	1995
7	Australasian Stroke Trials Network	ASTN	Stroke	1996
8	Australia & New Zealand Melanoma Trials Group	ANZMTG	Melanoma	1999
9	Australia New Zealand Gynaecological Oncology Group	ANZGOG	Gynaecological Cancer	2000
10	The Australasian Consortium of Centres for Clinical Cognitive Research	AC4R	Memory Loss/Dementia	2000
11	Therapeutic and Vaccine Research Program, Kirby Institute	TVRP	HIV & other Virus Diseases	2002
12	Australian & New Zealand College of Anaesthetists Clinical Trials Network	ANZCA CTN	Anaesthesia, Pain & Perioperative Medicine	2002
13	Paediatric Research in Emergency Departments International Collaborative	PREDICT	Paediatric Emergency Medicine	2004
14	Australasian Lung Cancer Trials Group	ALTG	Thoracic Cancer	2004
15	Psycho-Oncology Co-operative Research Group	PoCoG	Psycho-Oncology	2005
16	The Australasian Sleep Trials Network	ASTN	Sleep Research	2005
17	The Australasian Kidney Trials Network	AKTN	Kidney Disease	2005
18	Palliative Care Clinical Studies Collaborative	PaCCSC	Palliative Care Clinical Studies	2006
19	Australian Paediatric Research Network	APRN	General Paediatrics	2007
20	Cooperative Trials Group for Neuro-Oncology	COGNO	Brain Tumours	2007
21	Australian & New Zealand Urogenital and Prostate Cancer Trials Group	ANZUP	Urogenital & Prostate Cancer	2008
22	Australasian Sarcoma Study Group	ASSG	Sarcoma	2008
23	Australasian College for Emergency Medicine Clinical Trials Group	ACEM CTG	Emergency Medicine	2008
24	The Australian Spinal Cord Injury Network	ASCIN	Spinal Cord Injury	2008
25	Australasian Society for Infectious Diseases Clinical Research Network	ASID CRN	Infectious Diseases / Molecular Epidemiology	2009
26	Primary Care Collaborative Cancer Clinical Trial Group	PC4	Cancer Research in Primary Care	2009
27	NSW Better Treatments 4 Kids	BT4K	Paediatric Clinical Trials	2010
28	The Australian Type 1 Diabetes Clinical Research Network	T1DCRN	Type 1 Diabetes	2010
29	MS Research Australia Clinical Trials Network	MS RA CTN	Multiple Sclerosis	2010
30	Paediatric Trials Network Australia	PTNA	Paediatrics	2011
31	Australian Musculoskeletal Clinical Trials Group	AUSMUSC	Musculoskeletal Disorders	2013
32	Australian Primary Care Research network	APCReN	Primary Care	2013
33	Australian Epilepsy Clinical Trials Network	AECTN	Epilepsy	2013
34	Australasian Radiopharmaceutical Trials Network	ARTnet	Radiopharmaceuticals for Imaging/Therapy	2014

4.2 How and why did the networks form?

Networks were asked to identify one or more factors that had been key drivers for the formation of the networks. The responses provided by networks are displayed in Figure 4-1. By far the most commonly reported factor was drive by clinician researchers, which was identified by 33 networks. A key funding opportunity (n=7), support of a parent body (n=6) or the conduct of a single collaborative study (n=5) were also identified by multiple networks as key factors. One network reported that its formation was, in part, driven by an identified need from 'Government or a health agency', in association with a dialogue with the Pharmaceutical Benefits Advisory Committee, to develop clinical evidence related to the off-label use of medication. Another network identified linkage with non-clinical basic science as an important factor that led to its establishment.

FIGURE 4-1 KEY DRIVERS FOR THE FORMATION OF NETWORKS (N=34)



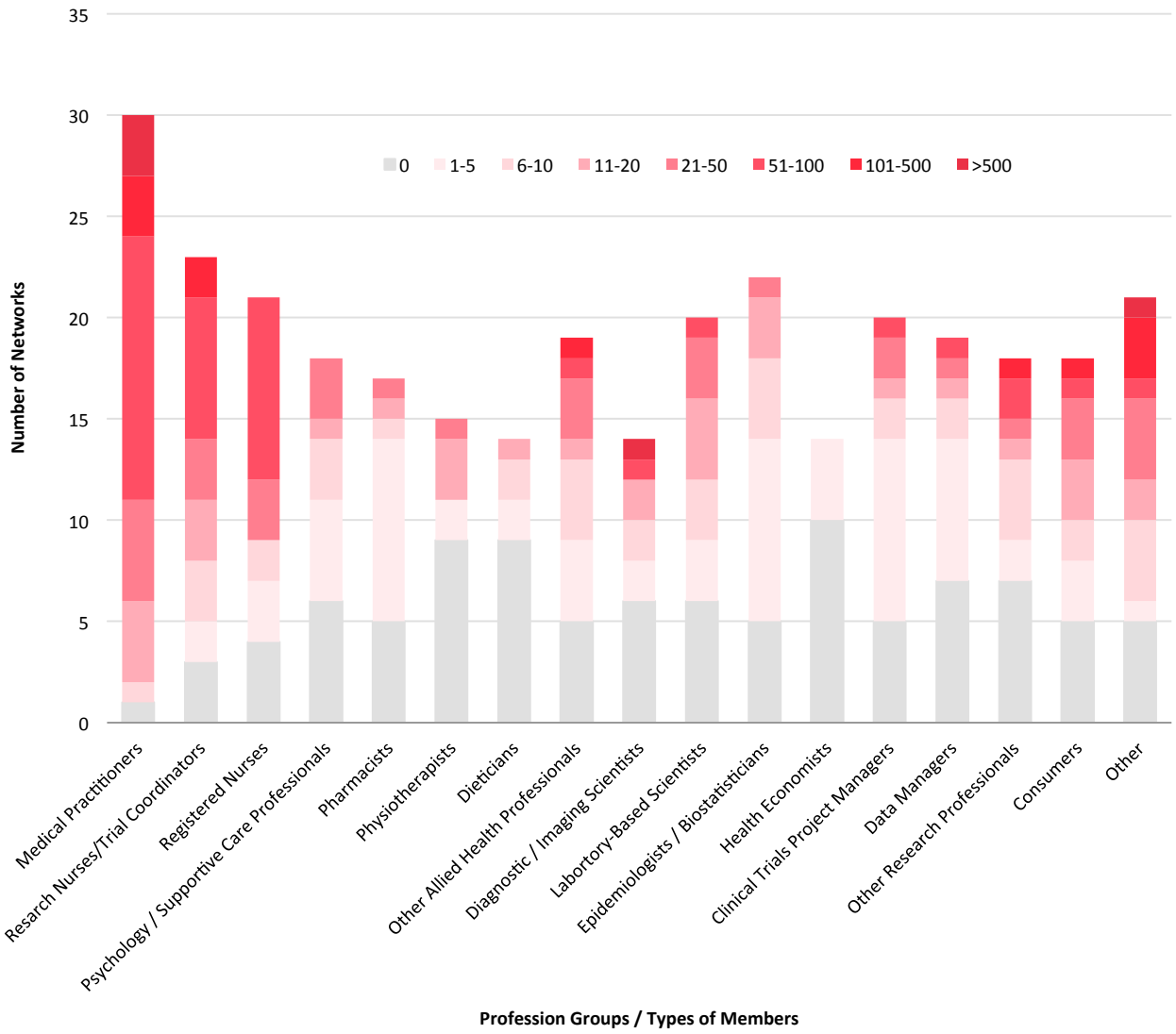
4.3 What types of membership models do networks have?

There were 18 networks that reported having a formal membership structure, although only three required the payment of membership fees. The remaining networks reported having an informal membership structure. Individual membership was offered by 32 networks while 12 networks offered membership to organisations such as hospitals or other institutions, and 11 offered membership to both organisations and individuals. Criteria for membership also varied with some networks requiring individuals to demonstrate a level of research success via publication or grant funding in order to be eligible for full membership, or for participating sites to demonstrate evidence of clinical and/or research proficiency. Some networks had forms of associate membership that were open to any interested person, including health consumers or industry representatives or both. Among the networks that were associated with Societies or Colleges, some reported that they restricted membership or leadership roles to members or Fellows.

Feedback received from networks during the planning stage of the survey indicated that few, if any networks, would be able to provide precise data for the exact number of individuals with different skillsets and backgrounds who contributed to network activities. For this reason, the survey asked networks to report an estimated range for the number of individuals from different professional groups or with different areas of expertise that are actively involved with the network. This precludes calculation of an exact number of individuals who contribute to the networks. However, the ranges reported for the number of individuals in each professional/expertise category is displayed in Figure 4-2.

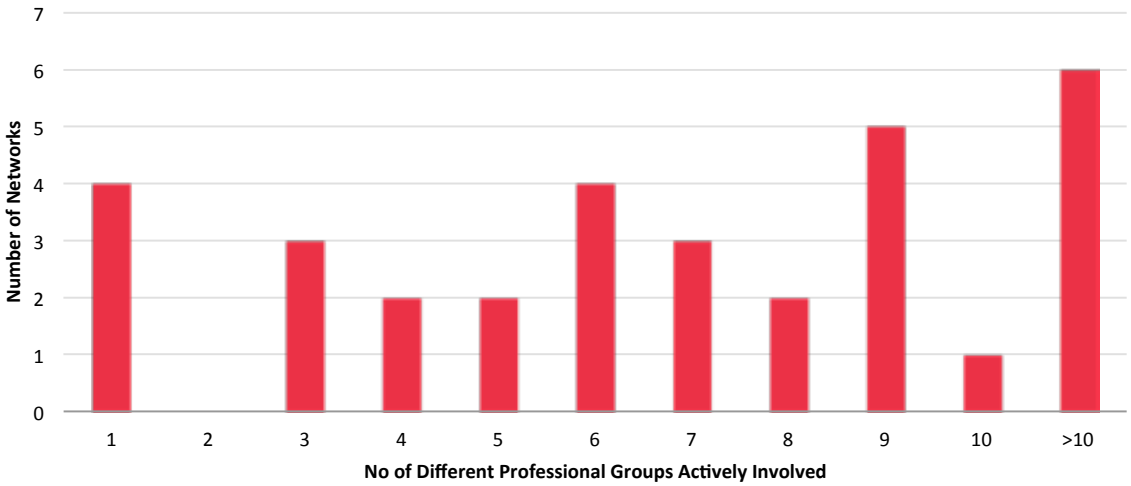
Medical Practitioners were the most heavily represented professional group reported to be actively involved in 31 networks (97%) with two networks reporting >500 medical practitioners and three networks reporting between 100 and 500 medical practitioners. Also heavily represented were Research Nurses and Trials Coordinators, Registered Nurses, Allied Health Professionals, Diagnostic and Imaging Specialists, Clinical Trial Project Managers, Data Managers and other Research Professionals. A total of 13 networks acknowledged the active involvement of consumers in the network.

FIGURE 4-2 NUMBER OF ACTIVE MEMBERS BY PROFESSIONAL GROUP (N-32)



The diversity of different professional groups involved in networks is shown in Figure 4-3. Well over half of the networks (n=23) reported having five or more different professional groups actively involved in the network. Of these, six networks reported that more than 10 different professional groups were actively contributing to the networks' research.

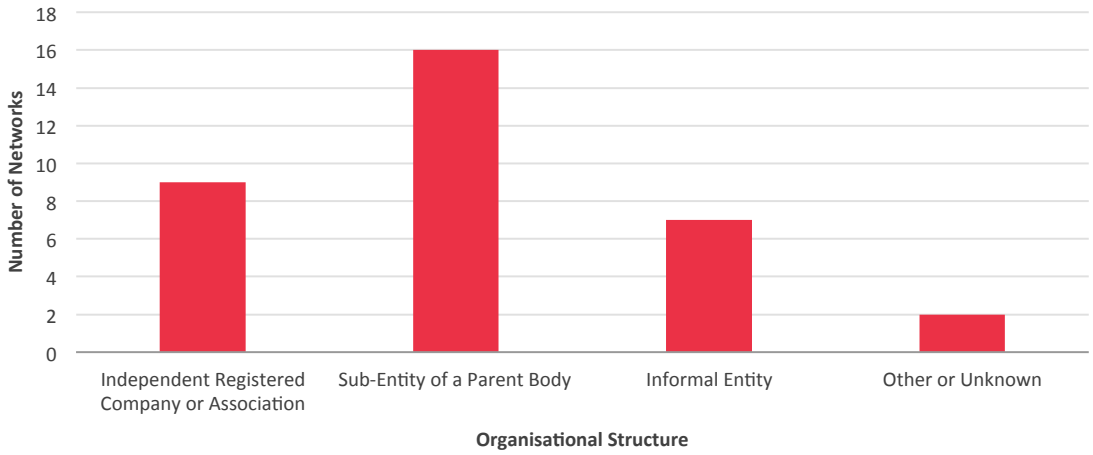
FIGURE 4-3 DIVERSITY OF PROFESSIONAL GROUPS ACTIVELY INVOLVED IN NETWORKS (N=32)



4.4 What types of organisational structures do networks have?

The type of organisational structures adopted by networks is shown in Figure 4-4. Among the participating networks, 16 identified as being a sub-committee or component of a parent organisation such as a professional society or a college, nine were independently registered companies or associations, and seven reported being a loose or informal entity. Of the nine networks that were independently registered companies or associations, eight networks reported that they were registered as a charity and able to receive tax deductable gifts for the purpose of fundraising.

FIGURE 4-4: STRUCTURE OF NETWORKS (N=34)



4.5 How do networks coordinate central administration?

The infrastructure available to support central administration varied substantially among participating networks. There were 22 networks that maintained a physical office that was solely or predominantly dedicated to the network and 28 that reported having an Executive Officer or Senior Manager/Administrator for the network.

There were 8 networks that reported having no paid staff members that were responsible directly to the network. Across the 26 networks that did have paid staff, there was a total of 181.5 Full Time Equivalent (FTE) staff reported, but with a median (IQR) of 1.9 FTE (0.8 - 3.6) per staffed network. Funding to support network staff was predominantly provided directly via the network (median [IQR] 100% [85 – 100]).

Half of the FTE supported by staffed networks was dedicated to supporting central administration of the network (median [IQR] 50% [25 – 80]). A summary of the remaining FTE usage is provided in Table 4-2. Other activities undertaken by paid staff included development of project concepts, general network development, research support for a parent body, and strategic planning.

TABLE 4-2: UTILISATION OF FTE BY STAFFED NETWORKS (N =26)

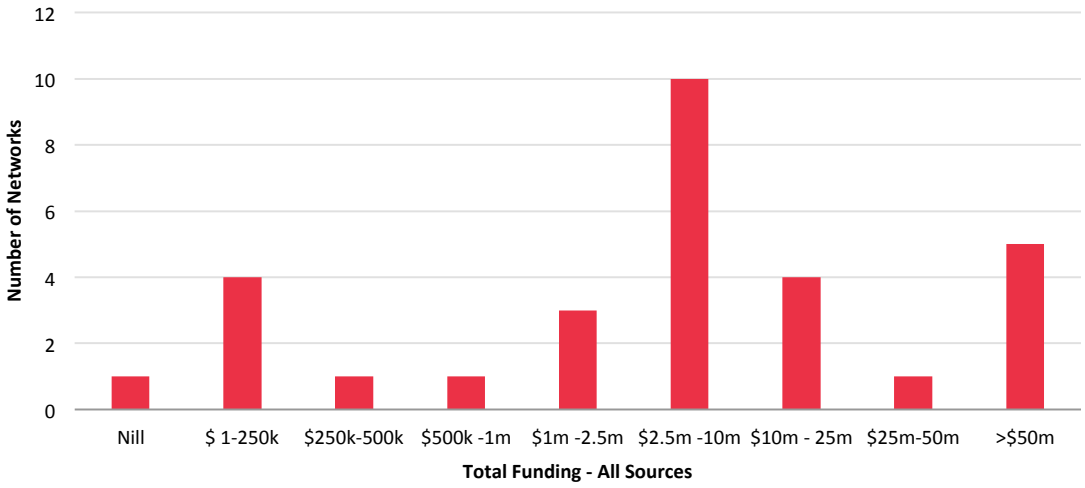
Network Activity	No of Staffed Networks Reporting FTE per Activity	Total FTE Reported (all staffed networks)	% of Total FTE per Staffed Network (Median [IQR])
Central Network Administration	26	31.39	50% [25.25 - 80]
Research Project Management	16	59.01	20% [0 - 40]
Training/Education	13	17.14	1.5% [0 - 20]
Charitable Fundraising	6	5.02	0% [0 - 0.25]
Consumer Engagement	11	3.86	0% [0 - 10]
Other Activities	7	2.09	0% [0 - 6.25]
Total		**118.51 FTE**	

4.6 How are networks funded?

4.6.1 Total funding generated by networks to date

Networks were asked to provide an estimate of the total funding they had generated since their inception from all sources including competitive grants, philanthropy and commercial funding. The results are presented in Figure 4-5. The median total funding generated by networks was in the range of $2.5 to 10 million. There were five networks that reported that they had generated between $10- 50 million and a further five networks reported more than $50 million in total funding.

FIGURE 4-5: TOTAL FUNDING GENERATED BY NETWORKS IN THE LAST 10 YEARS FROM ALL SOURCES (N= 30)



Central administration costs and sources of funding

The amount of total funding that was directed towards central administration of the network (as opposed to research project funding) is shown in Figure 4-6. The median expenditure on central network administration was reported to be between $100,000 and $250,000 per year. There were 11 networks with central administrative costs that lay between $100,000 and $500,000. The diverse range of different sources of funds that were used to support central network administration costs is outlined in Figure 4-7.

Government Grants (other than NHMRC grants) were the most frequently cited source (n=14) and this is largely owing to the provision of funding by Cancer Australia to 13 National Cancer Cooperative Trials Groups, of which 12 participated in this study. Other frequently cited sources included funding from a parent body (n=7 including descriptions provided in "other sources"), NHMRC Grants (n=6), State Government Grants (n=6) and Industry (n=6). One network reported generating funds for central administration through fees charged for the scientific review of clinical trial protocols.

FIGURE 4-6: ANNUAL EXPENDITURE FOR CENTRAL NETWORK ADMINISTRATION (N =31)

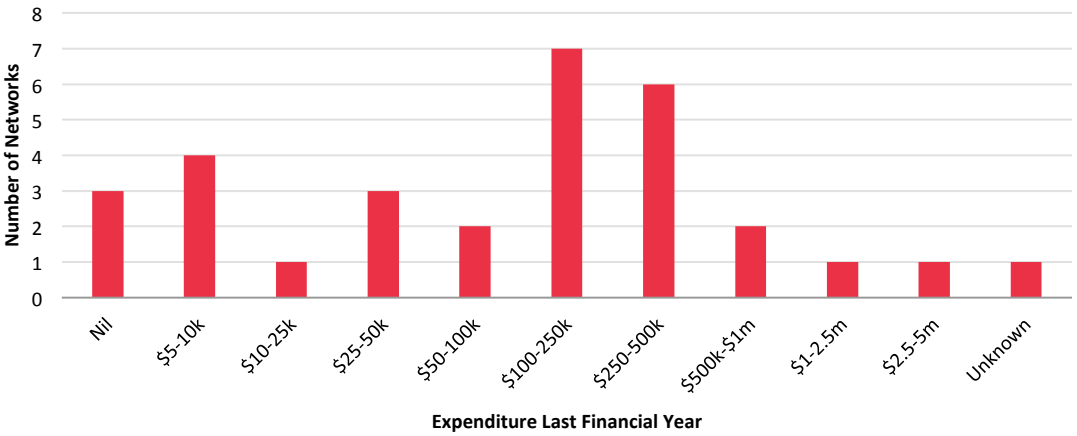
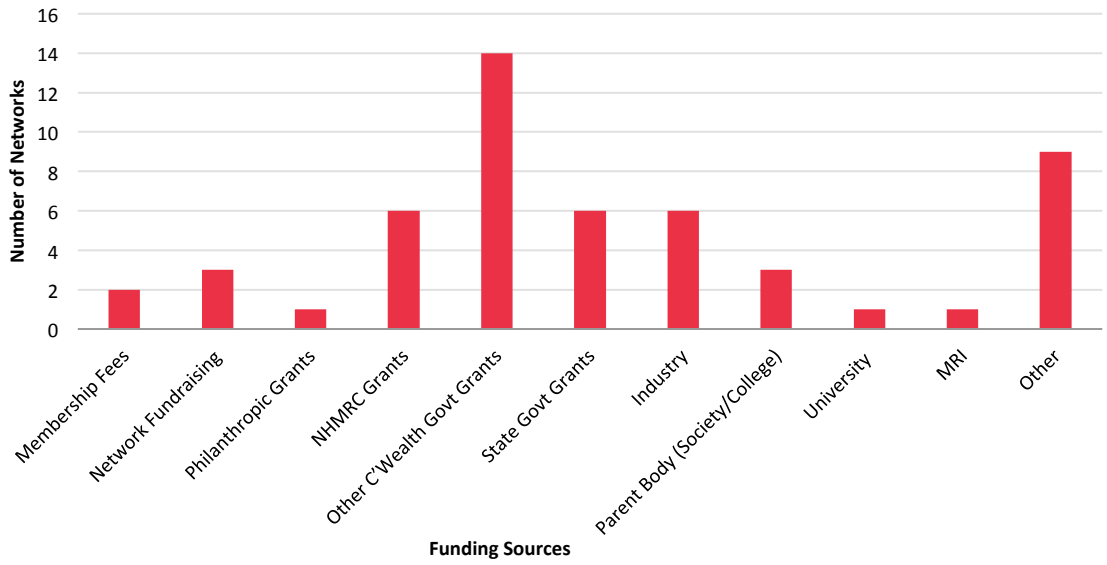


FIGURE 4-7 MAJOR FUNDING SOURCES FOR CENTRAL NETWORK ADMINISTRATION (N =31)



4.7 What activities do networks undertake?

There was substantial variation in the range of activities undertaken by networks to support the research that they conduct. The activities undertaken by networks and the number of networks reporting each of these types of activities are displayed in Figure 4-8. The most frequently reported activities were collaborative development and peer review of research proposals (n=29 and n=26, respectively). Convening and organising scientific meetings, providing education and training for researchers, grant writing, and study protocol development were all undertaken by more than 20 participating networks. Less frequently reported were charitable fundraising and advocacy (both n=9) and clinical guideline development (n=7).

4.7.1 Different organisational models adopted by networks

Analysis of these data indicates that there are, broadly, two main models of undertaking research that have been developed by networks (see Box 2). In one model, which has been classified for the purpose of this report as a 'Facilitating Network', the network facilitates the collaborative development and funding of studies, but generally has little or no direct role in the day-to-day management and coordination of clinical trials.

The second model, dubbed a 'Coordinating Network', involves the network also taking on the role of coordinating clinical trials and providing direct project management for aspects of trial conduct such as regulatory affairs, site liaison and management, recruitment, monitoring, data management, and statistical analysis.

For groups that use the Facilitating Network model, the work associated with conducting trials, such as project and data management, is devolved to a relatively small number of specialist trial coordinating centres that are generally based either in MRIs or University departments.

Approximately half of the participating networks (n=18) reported having direct involvement in clinical trial coordination or project management and have therefore been classified for the purpose of this report as 'Coordinating Networks'. The remaining 16 networks have been identified as having adopted a 'Facilitating Network' model. Analysis of the relationship between different models and network achievements was beyond the scope of this report but future research to provide insights in this area would be of substantial value.

4.7.2 Collaboration with Clinical Trial Coordinating Centres

All networks were asked to identify any Trial Coordinating Centres/Methods Centres that they had collaborated with to conduct clinical trials. A list of all centres that were identified, including international centres, is provided in Table 4-3. These centres represent a vital component of the national infrastructure that supports the conduct of clinical trials conducted by networks.

Box 2. Clinical Trial Network Models

Facilitating Networks

Undertake many or all of the following:

- Identify important clinical questions
- Collaborative development & peer review of studies
- Study protocol development
- Formal endorsement of studies (+/-manuscripts)
- Scientific meetings
- Education/training/mentoring for clinician researchers
- Grant writing
- Liaison with consumers
- Liaison with industry
- Fundraising
- Research advocacy
- Clinical guideline development
- Assistance with site selection
- High-level trial oversight via a Management Committee
- Coordination of Data Safety Monitoring Boards
- *Do not undertake direct study coordination*
- *Do not act as the study sponsor*

Coordinating Networks

Undertake many or all of the activities of a Facilitating Network plus:

- Direct Trial Coordination/Project Management
- Regulatory Affairs
- Site Management
- Recruitment
- Monitoring
- Data Management
- Statistical Analysis
- May or may not also act as the study sponsor

FIGURE 4-8: ACTIVITIES UNDERTAKEN BY NETWORKS (N=34)

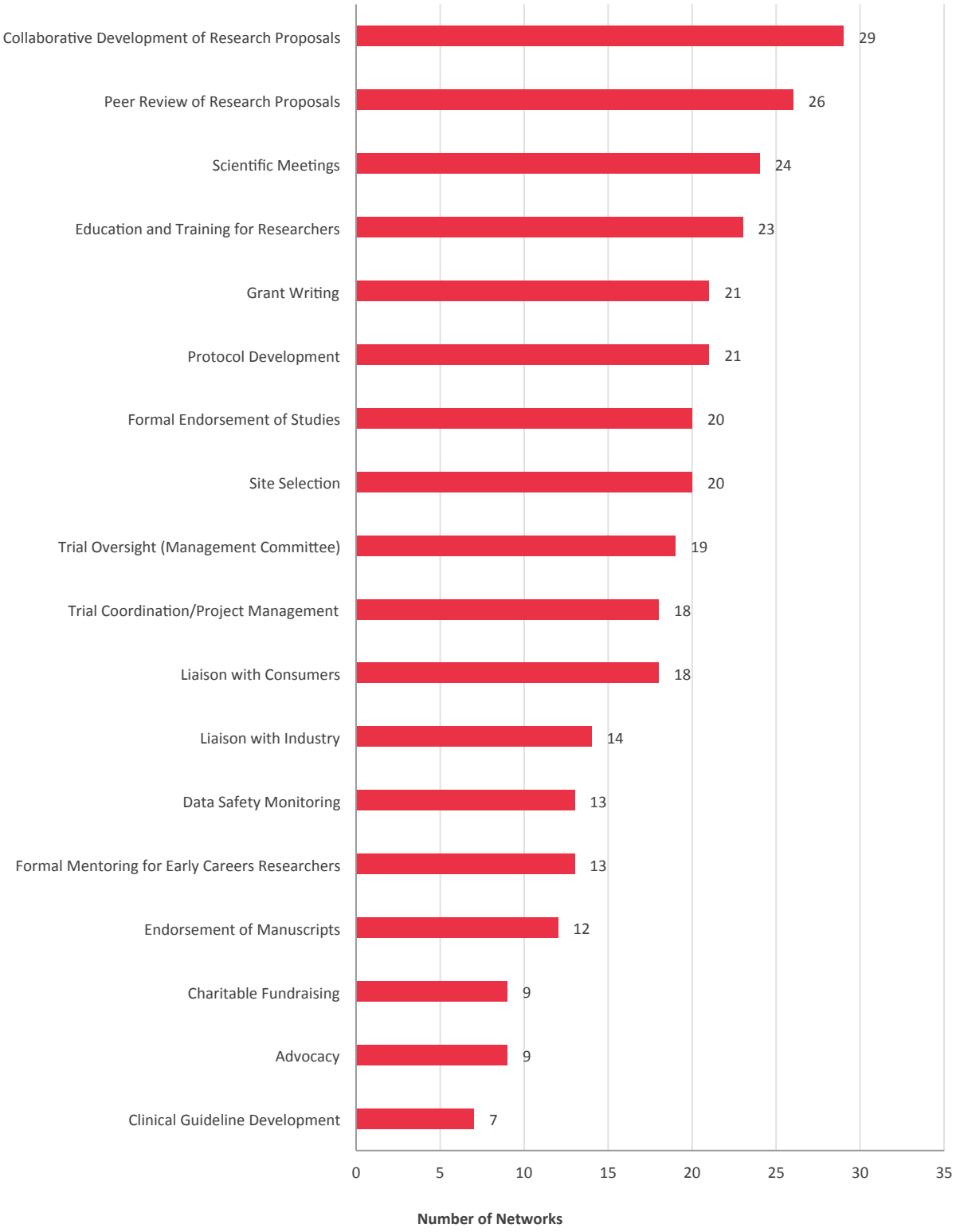


TABLE 4-3 COORDINATING CENTRES THAT COLLABORATE WITH AUSTRALIAN NETWORKS

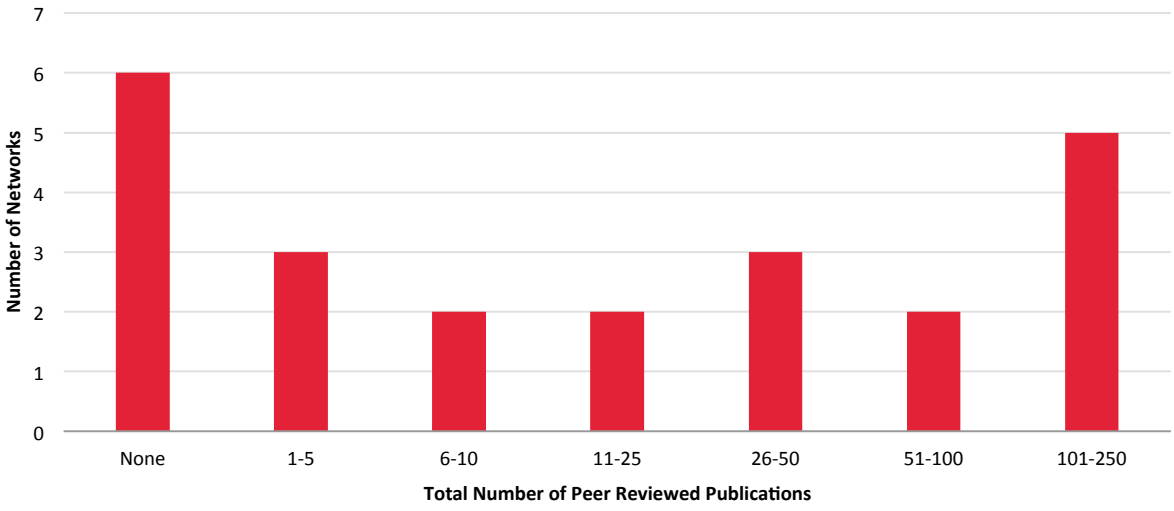
Trial Coordinating Centre*	City	State	Country
ANZIC Research Centre, Monash University	Melbourne	VIC	Australia
Auckland Regional Cancer and Blood Service, University of Otago	Wellington	-	NZ
Birmingham Clinical Trials Unit	Birmingham	-	UK
Centre for Biostatistics and Clinical Trials, PeterMac	Melbourne	VIC	Australia
Chinese University of Hong Kong	Hong Kong	-	China
Cleveland Clinic	Cleveland	Ohio	USA
Deakin University	Melbourne	VIC	Australia
Epilepsy Study Consortium, Inc.	Woodbury	New Jersey	USA
Hamilton Health Sciences	Hamilton	Ontario	Canada
Hunter Medical Research Institute	Newcastle	NSW	Australia
Monash University	Melbourne	VIC	Australia
Murdoch Children's Research Institute	Melbourne	VIC	Australia
NCIC Clinical Trials Group	Kingston	Ontario	Canada
Neuroscience Trials Australia	Melbourne	VIC	Australia
NHMRC Clinical Trials Centre	Sydney	NSW	Australia
Ontario Clinical Oncology Group	Hamilton	Ontario	Canada
Population Health Research Institute	Hamilton	Ontario	Canada
Queen Mary University of London	London	-	UK
Queensland Clinical Trials and Biostatistics Centre	Brisbane	QLD	Australia
Royal Victoria Hospital	Montreal	Quebec	Canada
The European Organisation for Research and Treatment of Cancer	Brussels	-	Belgium
The Florey Institute of Neuroscience and Mental Health	Melbourne	VIC	Australia
The George Institute for Global Health	Sydney	NSW	Australia
The Institute of Cancer Research Clinical Trials and Statistics Unit	London	-	UK
Toronto General Hospital	Toronto	Ontario	Canada
University of New South Wales	Sydney	NSW	Australia
University of Newcastle	Newcastle	NSW	Australia
University of Queensland	Brisbane	QLD	Australia
University of Western Australia	Perth	WA	Australia

*NB: Excludes hospital-based trial centres in Australia; * - colour was used to distinguish between Australian (black font) and International (red font) collaborations*

4.7.3 Level of research activity among networks

A more detailed report on the studies conducted by networks over the last decade is provided later in this document. However, as a high-level indication of the level of their of research activity, networks were asked to identify how many peer-reviewed articles that network had published in the last 10 years (publication date 2004-2014). Figure 4-9 shows the ranges of the total number of peer-reviewed articles reported per network. There were five networks that reported between 101 and 250 publications during this time.

FIGURE 4-9: TOTAL NUMBER OF PEER REVIEWED ARTICLES PUBLISHED BY NETWORKS (N=23)



4.8 What links do networks have with healthcare and research facilities?

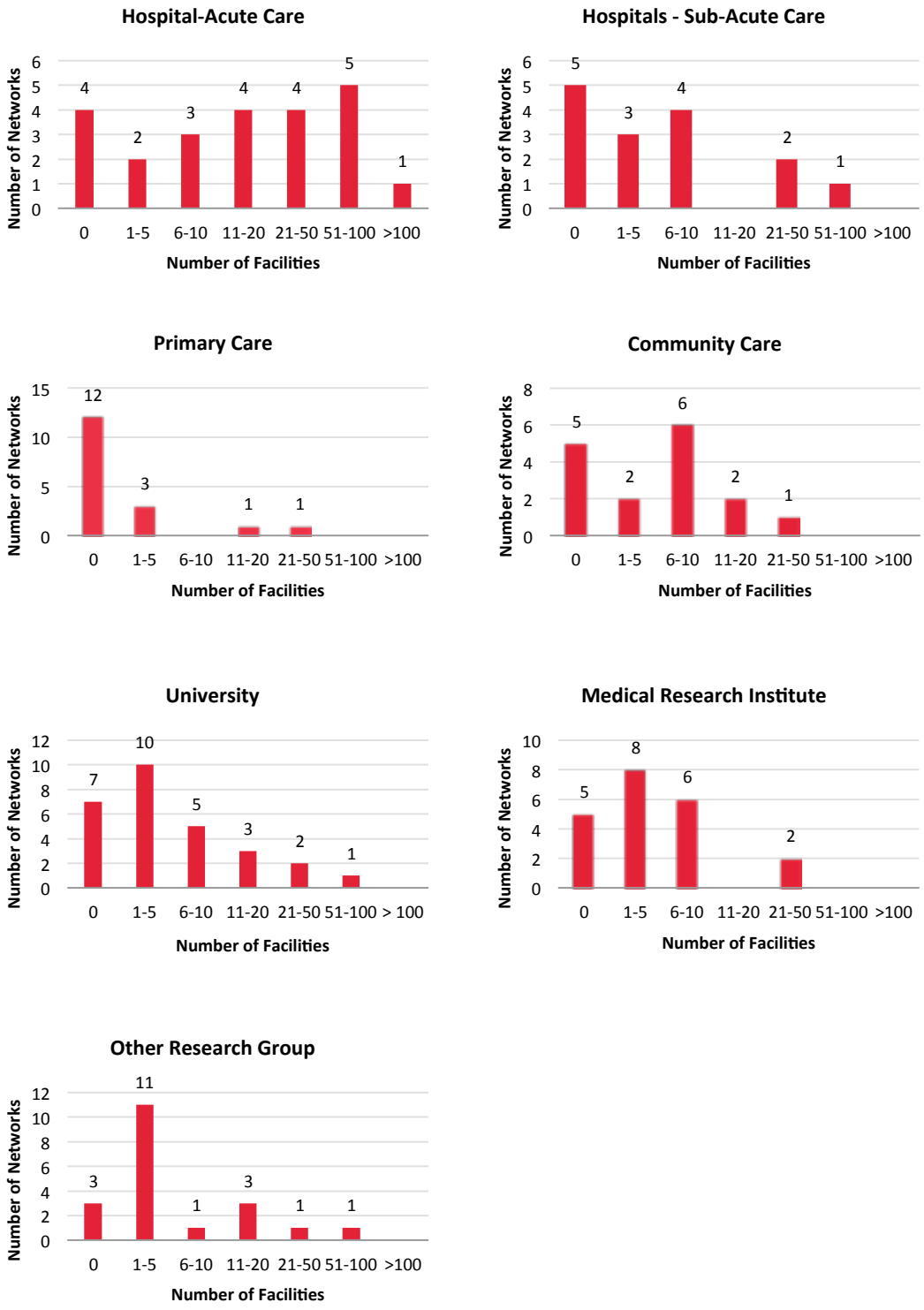
4.8.1 Healthcare settings

Networks were asked to indicate the approximate number of different types of healthcare facilities and academic or research centres that were directly involved in the network. Overall, 30 networks were able to provide this information. The number of networks with linkage to different health care settings and academic partners included Acute Care Hospitals (n=20), Sub-Acute Hospitals (n=9), Primary Care Facilities (n=5), Community Care Facilities (n=4), Universities (n=19), MRIs (n=17) and Other Research Groups (n=20).

4.8.2 Research facilities

Figure 4-10 shows the number of linkages of the networks to each type of facility that was reported. There were six networks that had active involvement with more than 50 Acute Care Hospitals, and three networks with direct links to more than 20 Sub-Acute Hospitals. Five and four networks reported the active involvement of Primary Care and Community Care Facilities, respectively. There were 21 networks that reported the active involvement of one or more Universities, and 16 networks reported links with one or more MRIs. There were 13 networks that reported having established links with bio-banking facilities for a total number of 98 different studies.

FIGURE 4-10: NUMBER OF HEALTHCARE AND RESEARCH FACILITIES ACTIVELY INVOLVED IN NETWORKS (N=32)

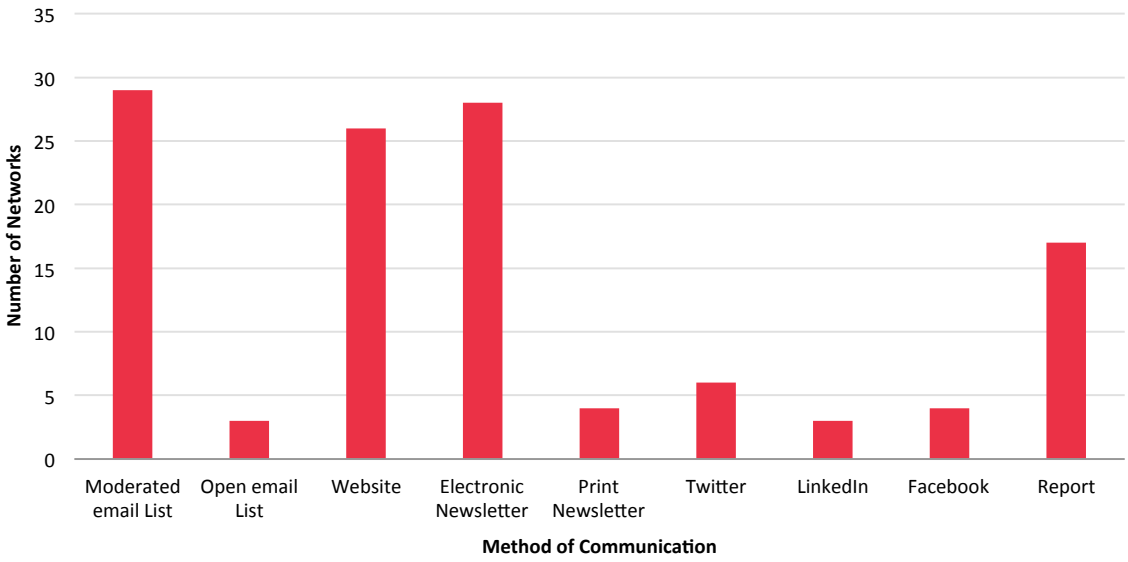


4.9 How do networks engage with their members and stakeholders?

4.9.1 Communication tools used by networks

Networks reported using a variety of different methods to communicate with their members and stakeholders and these are shown in Figure 4-11. The most frequently reported methods were a moderated email list (n=29 networks), electronic newsletter (n=28), website (n=26) or via formal report (n=17). Relatively few networks reported using social media platforms to communicate with members. Among those that did use social media as a communication tool, Twitter was the most frequently reported social media platform (n=6), followed by Facebook (n=4) and LinkedIn (n=3).

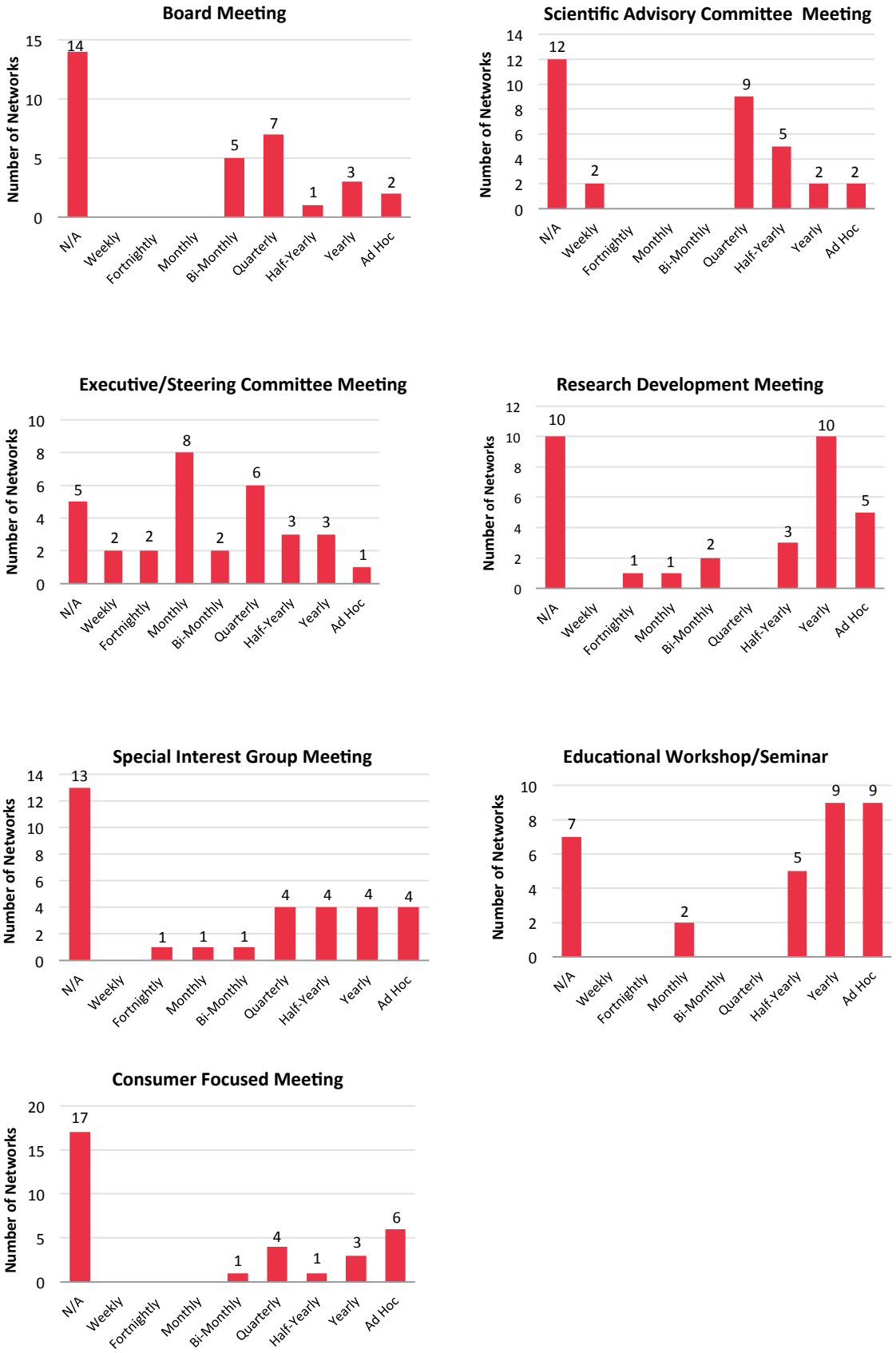
FIGURE 4-11: COMMUNICATION TOOLS USED BY NETWORKS



4.9.2 Methods of supporting collaboration

Many networks identified meetings as a key method of enabling collaboration between their members. The range of different types of meetings, and the frequency with which they were held, is displayed in Figure 4-12. The majority of networks hold regular meetings to support collaborative research development including Scientific Advisory Committee Meetings (n=18), Research Development Meetings (n=17), Executive/Steering Committee Meetings (n=27) and Special interest Groups Meetings (n=15). There were 16 networks that reported holding regular educational workshops and seminars. Only nine networks reported holding regular meetings with consumers, with the reminder reporting that these were either held *ad hoc* or not at all.

FIGURE 4-12: FREQUENCY OF MEETINGS HELD BY NETWORKS (N=32)



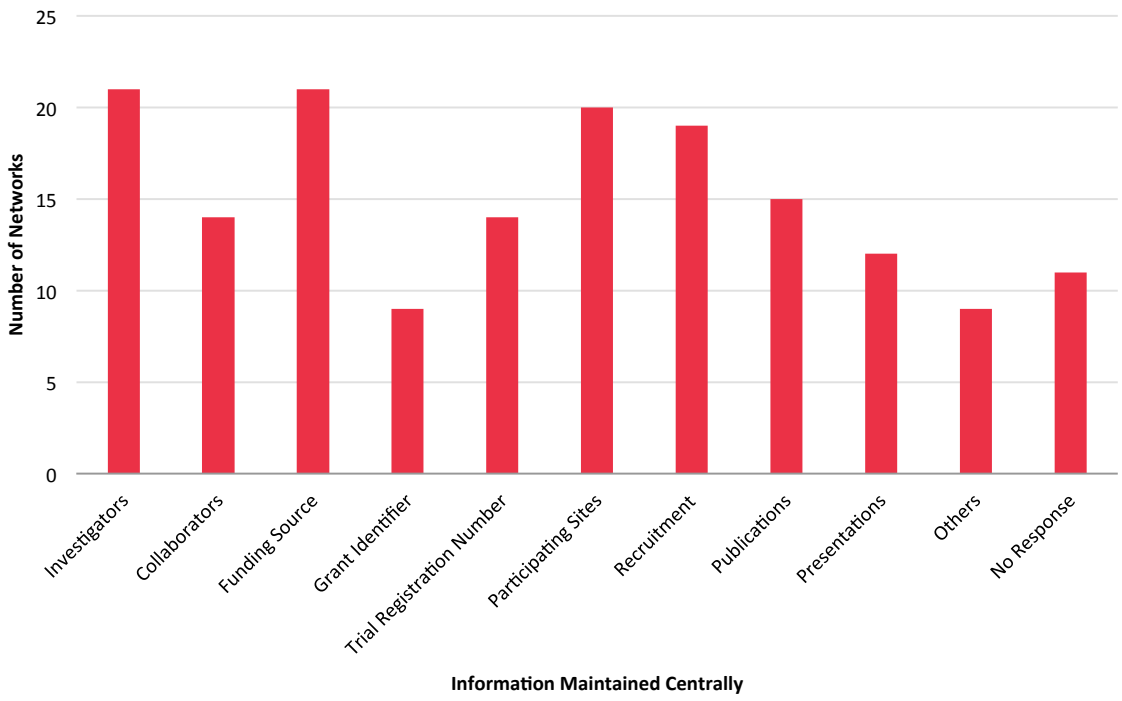
4.10 What information do networks maintain about their research?

4.10.1 Central administrative records

The information that networks maintained about their research activity varied substantially. There were 13 networks that indicated that they did not maintain a database of their research projects and related outputs (publications/presentations). Among the 19 networks that did maintain a central repository of information about their research activity, the types of details kept are shown in Figure 4-13.

Several of these networks have established systems for keeping the information that is maintained in their databases accurate and up to date. However, many of these networks indicated that their information is either incomplete or delayed, sometimes being dependent on the investigators who are responsible for each project providing updated information to the central network database. While a small number of networks reported using trial-related databases, only four of these networks reported using a purpose-built application or licensed software package for storing details about the network's research activity as a whole.

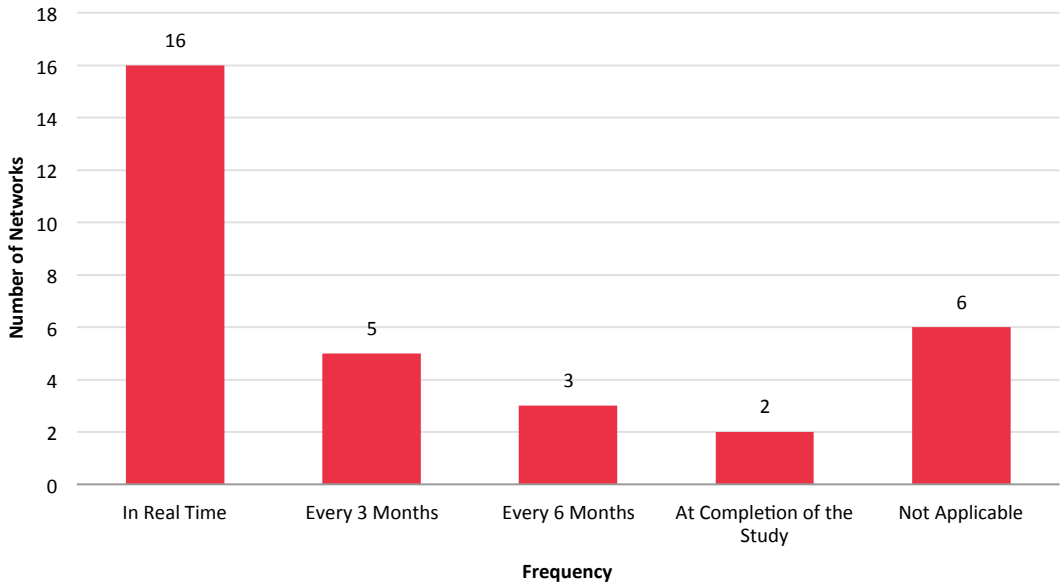
FIGURE 4-13: INFORMATION MAINTAINED BY NETWORKS ABOUT THEIR RESEARCH (N=21)



Capacity to report recruitment into clinical trials

Networks were also asked to indicate the timeframe in which they were able to provide information about recruitment into their studies and these responses are shown in Figure 4-14. Only half (15 networks) indicated that they were able to report recruitment figures in real-time or near real-time.

FIGURE 4-14: CAPACITY OF NETWORKS TO REPORT RECRUITMENT (N=32)



4.11 Where does network research activity occur?

4.11.1 Regional distribution of network members

Where the information was available to them, networks were asked to provide an estimate of the geographical distribution of people who are actively involved in the network. The aggregate distribution of active members across the 25 networks that were able to provide an estimate is reported in Figure 4-15 and is as follows: New South Wales 31.6%, Victoria 23.8%, Queensland 13.3%, Western Australia 8.4%, South Australia 6.5%, Australian Capital Territory 1.9%, Tasmania 1.7% and Northern Territory 0.9%. A further 5.6% of active members were reported in New Zealand and 6.6% from other international locations. Within Australia, the distribution of network members appears to generally mirror the general population distribution between the states and territories.

4.11.2 Regional distribution of recruitment into clinical trials

There were 21 networks that were able to estimate the proportion of recruitment into all of their studies conducted over the last 10 years that occurred in metropolitan versus rural and regional Australia, in New Zealand, or in other international locations. Figure 4-16 shows the reported distribution of total recruitment among these regions: 67% of the participants were recruited from within Metropolitan Australia (reported by 22 networks), 11% from Rural or Regional Australia (reported by 18 networks), 7% from New Zealand (reported by 9 networks) and 15% from other International Sites (reported by 9 networks). Of note, there was one network that reported 94% of its recruitment had come from international sites, which included New Zealand.

FIGURE 4-15: GEOGRAPHICAL PROFILE OF NETWORK MEMBERS (N=25 NETWORKS)

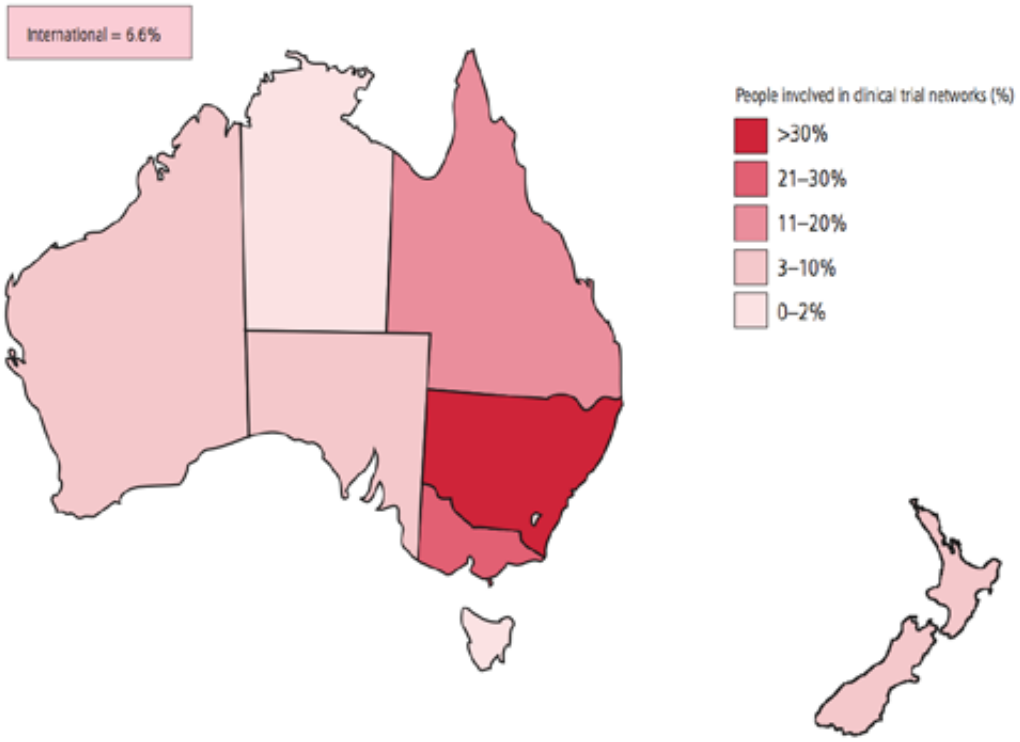
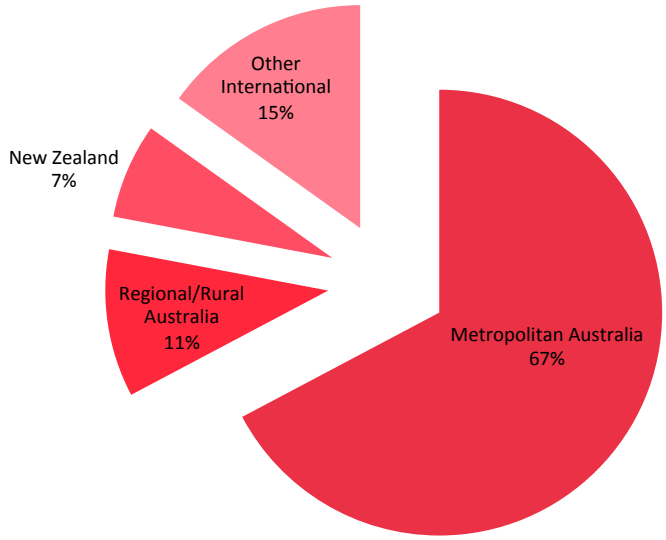


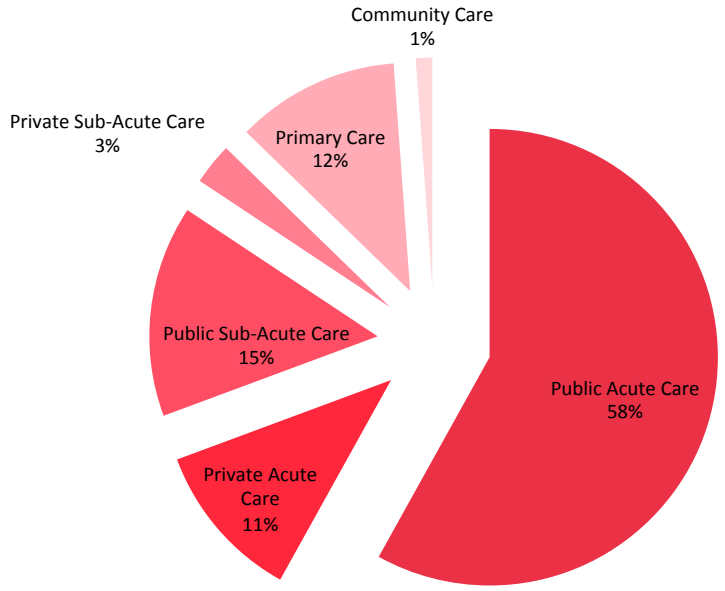
FIGURE 4-16: ESTIMATED GEOGRAPHICAL DISTRIBUTION OF TOTAL RECRUITMENT INTO NETWORK STUDIES (N=21)



4.11.3 Distribution of recruitment into clinical trials for different healthcare settings

There were 20 networks that were able to estimate the proportion of recruitment into their studies that occurred in different healthcare settings. For these networks, the distribution (weighted equally for each network) of their recruitment is displayed in Figure 4-17. The majority of recruitment reported was from within public acute care facilities (58%), followed by public sub-acute facilities (15%), primary care facilities (12%), private acute care facilities (11%), private sub-acute facilities (3%), and only a small proportion, (1%), from community care facilities.

FIGURE 4-17: ESTIMATED DISTRIBUTION OF TOTAL RECRUITMENT INTO NETWORK STUDIES BY HEALTHCARE SETTING (N=20)



4.12 Summary of key findings

- There were 37 different clinical trial networks identified in Australia, of which 34 (92%) contributed to this report. Many of these networks have only been established relatively recently with half of all networks formed in last 8 years. Almost all networks surveyed indicated that they were 'self-formed', largely in response to a perceived need by clinicians.
- There was substantial diversity in the membership structure, governance, and activities undertaken by networks but common to almost all networks is the key role of enabling the collaborative development and internal peer-review of project proposals.
- Two broad models of network structure were reported- facilitating networks that do not undertake direct trial management and coordinating networks that do undertake direct trial management.
- It was not possible to ascertain the exact number of individuals who contribute to network activities but this number is likely to exceed 10,000 individuals - the vast majority of whom are healthcare practitioners who both undertake research and deliver frontline healthcare.
- An important finding is that only a minority of networks reported supporting forums for actively engaging with health consumers. This area of potential growth for many networks.
- Almost all networks have an Executive Officer or Senior Manager but the median number of full time equivalent staff per network is only 1.9 FTE.
- The estimated median total research funding generated to date per network was $2.5 to 10 M, but this ranged from $10 to 25 M for 4 networks, $25 to 50 M for 1 network, and more than $50 M for 5 networks.
- There was quite substantial variability in the capacity of networks to report research inputs and outputs. Only 23 networks maintained a database of their activities and 16 networks were able to report recruitment in near real-time, with other networks only able to report recruitment with a lag period or at the completion of projects.
- There is extensive integration of networks with acute and sub-acute hospitals as well as primary and community care facilities. Research conducted by networks is embedded or integrated with routine healthcare delivery.

5

Studies Completed and Published by Australian Clinical Trials Networks 2004 - 2014

5 Studies Completed and Published by Australian Clinical Trials Networks 2004 - 2014

5.1 Notes on interpreting these results

For the purpose of this report, **Completed Published Studies** refers to a stand-alone study for which the primary results were published between 2004 and 2014.

Study category
The term **study category** refers to a classification of completed studies comprising:

- phase II, III, or IV clinical trials (reported as a single group);
- phase I clinical trials;
- pilot or feasibility trials;
- observational studies; and
- other study types (e.g. surveys)

This study did not seek to distinguish among phase II, III, and IV clinical trial as preliminary work with the networks identified that the definitions for each of these phases were not standardised (e.g. phase III and IV trials were at times used interchangeably) and would have been reported differently among the networks.

Completeness of the data
Each analysis has been conducted only using the valid data available for that analysis (no assumptions are made for missing values) with the number of valid records available to be analysed being reported for each figure. The completeness of data varies substantially across different variables and this needs to be taken into account when interpreting the results presented.

Duplicate studies
Of the completed published studies reported, 12 studies were collaborations between two or more networks and each participating network provided information on these studies. These studies were analysed as duplicates (i.e. included only once, unless otherwise specified).

Sample size
There were inconsistencies in the way that sample sizes were reported for studies that involved international collaboration. Some networks reported only the subset of participants that had been recruited from sites in Australia, while others reported the total number of participants recruited, including those that were recruited overseas.

Approximate total funding
Networks were asked to provide the approximate total amount of funding (derived from all sources) for each completed published study. This information could only be obtained for around one third (n=145, 31%) of all of the completed published studies that were identified by networks. Consequently, funding figures are likely to substantially underrepresent the total amount of funding that has been generated by networks for completed studies.

The data are also substantially influenced by two completed published studies conducted by a single network, each with an estimated total funding of $100m, Moreover, although the network played a major

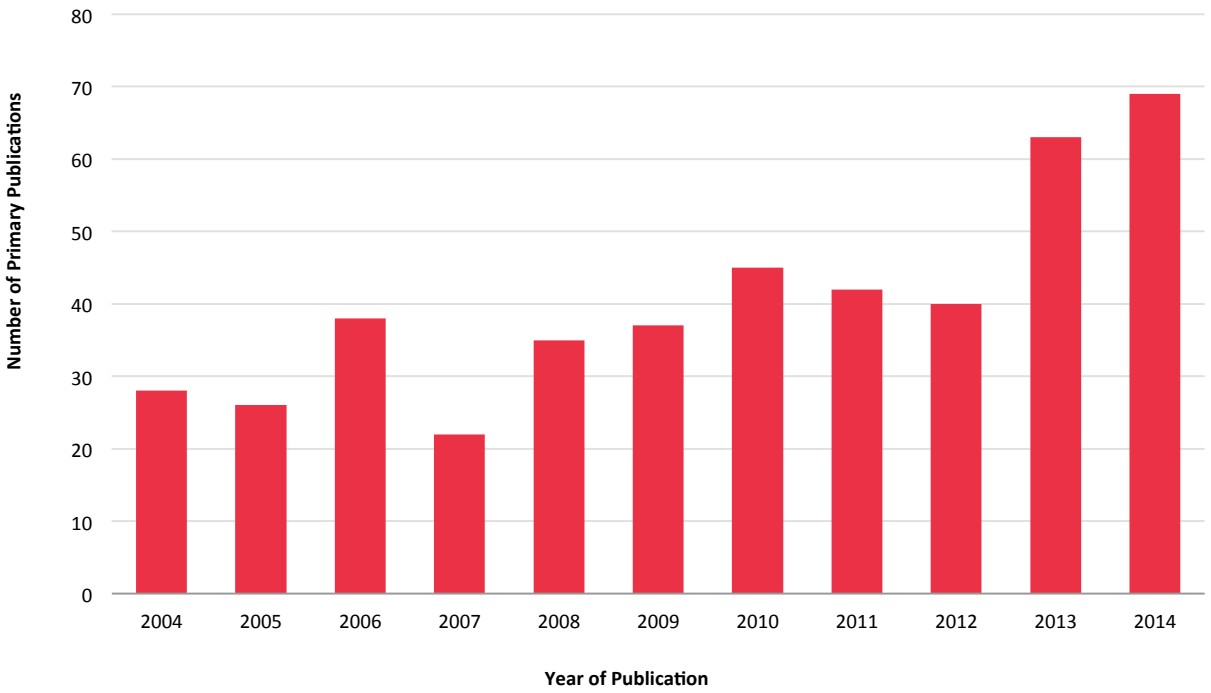
role in these large pivotal trials, the majority of the recruitment occurred at sites outside Australia. This funding has been retained within the analysis for two reasons: firstly, it was reported directly by the network; secondly, there were many networks that reported lesser amounts of funding from overseas sources that contributed to multinational studies and it was not possible to determine the proportion of recruitment that occurred in Australia or the proportion of funding that was expended in Australia. A decision was made to retain and report all funding identified, but figures should be interpreted in light of the amount of overseas funding for recruitment into trials outside Australia.

It should be noted that while there were a large number of studies for which even an approximate total funding amount was not known, these were not likely to be distributed evenly across primary funding sources as funding data were available to be cross tabulated for a much higher proportion of studies where the NHMRC was identified as the primary funding source. A more in-depth analysis of NHMRC funding for network studies is provided later in the report.

5.2 Number of completed published studies

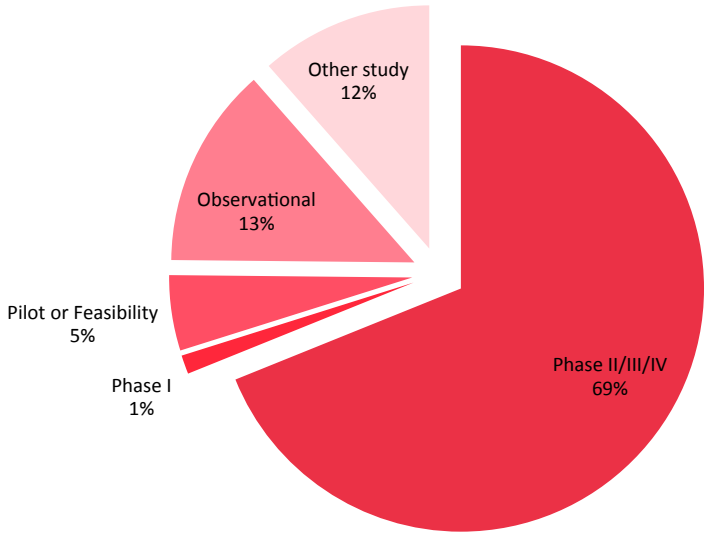
There were 467 completed published studies reported by participating networks between 2004 and 2014. The median (IQR) number of studies published per year among the 26 networks that reported having completed and published at least one study in the last 10 years was 38 (28 - 45) studies. As Figure 5-1 shows, the number of studies published by networks per year has more than doubled in the last 10 years from 28 studies published in 2004 to 69 studies published in 2014.

FIGURE 5-1: NUMBER OF COMPLETED PUBLISHED STUDIES PER YEAR (N=445)



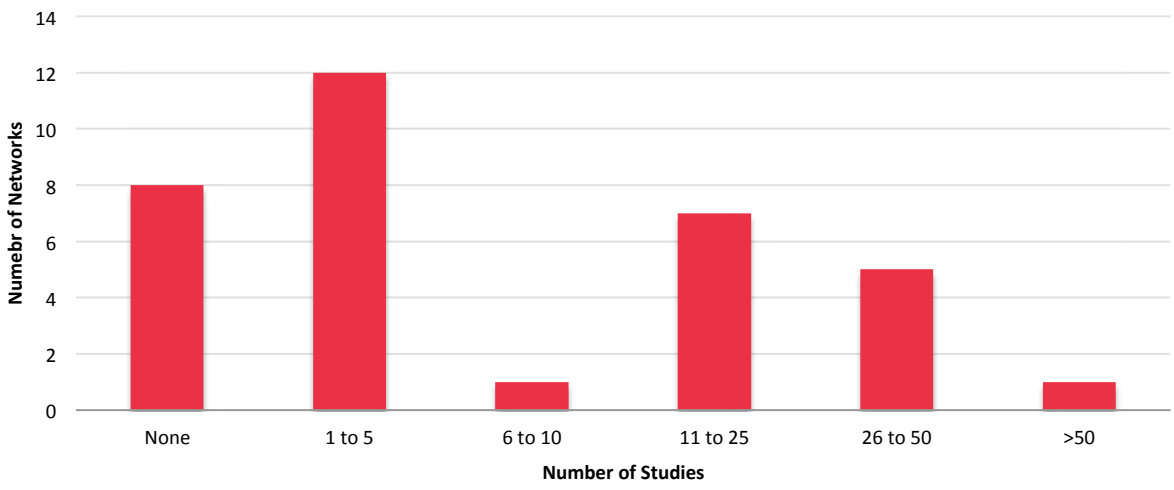
The proportion of different categories of studies published by networks is displayed in Figure 5-2. The vast majority of studies were phase II, III or IV clinical trials (n=321, 69%), followed by observational studies (n=62, 13%) and pilot or feasibility studies (n=24, 5%). Only 6 studies (1%) were identified as phase I clinical trials. There were 54 (12%) studies identified as 'Others' which included surveys, data audits, and basic science investigations.

FIGURE 5-2: NUMBER OF COMPLETED PUBLISHED STUDIES BY STUDY TYPE (N=467)



The distribution of completed published studies among all participating networks is displayed in Figure 5-3. The number of studies published per network ranged from 0 to 148 studies, with a median (IQR) of 3.5 (0.75 – 18) published studies per network. There were 8 networks that had not published a study; 12 networks that had completed and published between 1 and 10 studies; 7 networks that had published between 11 and 25 studies; 5 networks that had published between 26 and 50 studies and 1 network that had published more than 50 studies during the last decade.

FIGURE 5-3: NUMBER OF COMPLETED PUBLISHED STUDIES PER NETWORK (N=479 INCLUDES 'DUPLICATE' STUDIES)

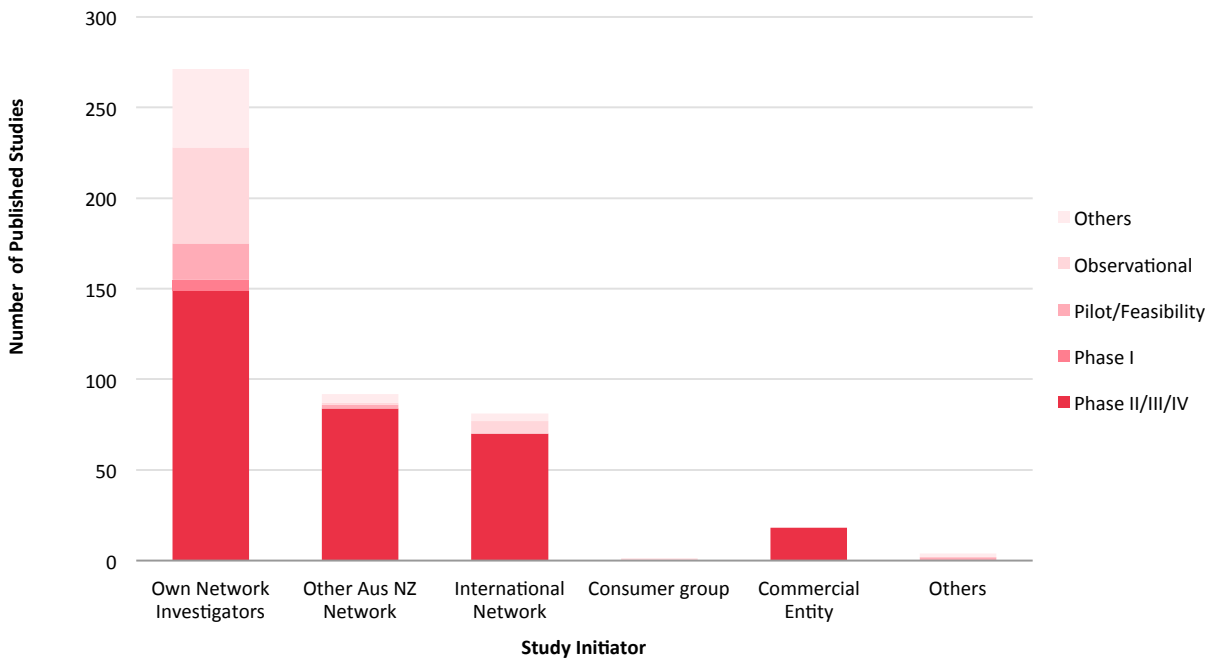


Networks were asked to identify the primary initiator of the study, classified as either:

- the network's own investigators;
- another Australian/New Zealand network;
- an international network;
- a consumer group;
- a commercial entity; or
- 'other'

These results displayed in Figure 5-4 show that the vast majority of published studies (where a study initiator was identified) were investigator-initiated (n=444, 95%). Of these, 227 (58%) studies had been initiated by the network's own investigators, 92 (20%) by another Australian/New Zealand network, and 81 (17%) by investigators from another international network. There were 18 (4%) studies initiated by a commercial entity. The remainder were initiated by a consumer group (n=1, 0.1%) or described as 'other' (n=4, 0.9%).

FIGURE 5-4: NUMBER OF COMPLETED PUBLISHED STUDIES BY STUDY INITIATOR (N=467)



Where the initiator of a study was known, the proportion of completed published studies with an academic/not-for-profit organisation as the sponsor was 90% (n=380), versus 10% (n=40) that were identified commercially sponsored studies (see Figure 5-5).

FIGURE 5-5: NUMBER OF COMPLETED PUBLISHED STUDIES BY STUDY SPONSOR (N=420)

5.3 Number of participants in completed published studies

The total reported number of participants aggregated across all completed published studies was 423,596. Of these, 341,833 participants were recruited into interventional studies (phase I-IV clinical trials and pilot/feasibility studies) and 81,763 into non-interventional studies (observational/other studies). The ranges of sample sizes for interventional and non-interventional studies published are shown in Figure 5-6 and Figure 5-7, respectively.

Among the interventional clinical trials (n=347), the number of participants raged from 1 – 26,499 with a median (IQR) sample size of 200 (63 – 635) participants per trial. There were 196 trials that recruited less than 250 participants, 91 trials recruited between 251 and 1,000 participants, 25 trials recruited between 1,001 and 2,500 participants, 17 trials recruited between 2,501 and 5,000, 11 trials recruited between 5,001-10,000 participants and 7 large trials recruited more than 10,000 participants.

There were several large non-interventional studies reported by networks, including 5 studies that involved between 1,001 – 2,500 participants, 5 studies that involved between 5,001 and 10,000 participants and 1 large observational study that involved 11,705 participants.

FIGURE 5-6: NUMBER OF COMPLETED PUBLISHED STUDIES BY SAMPLE SIZE – INTERVENTIONAL STUDIES (N=347)

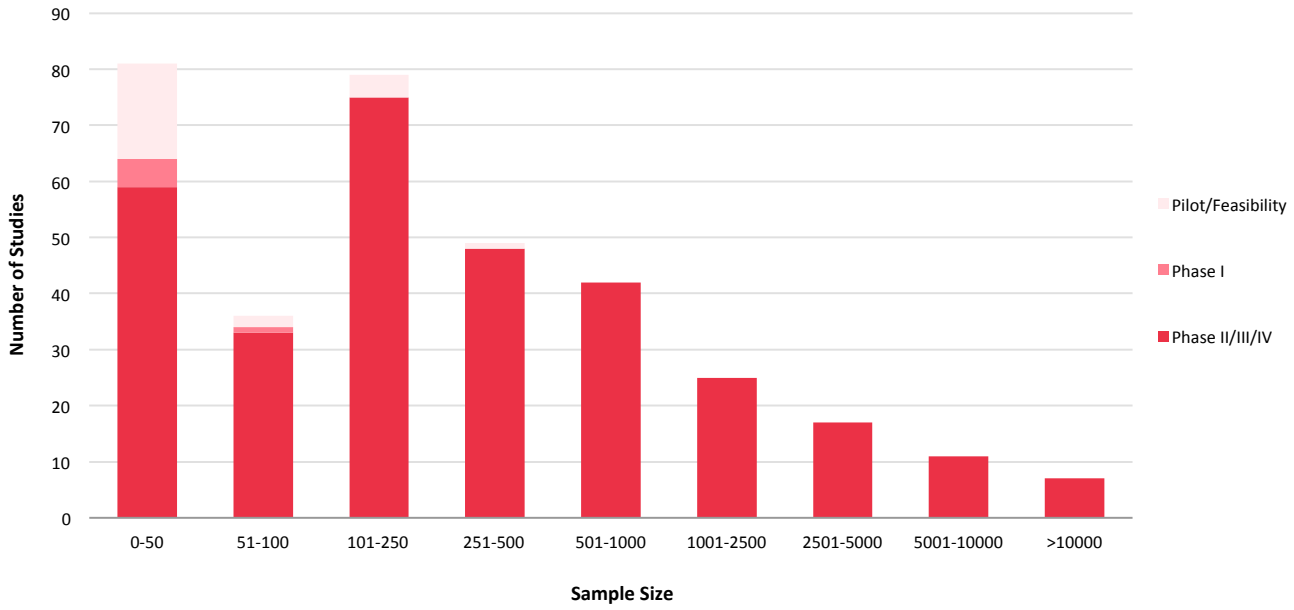
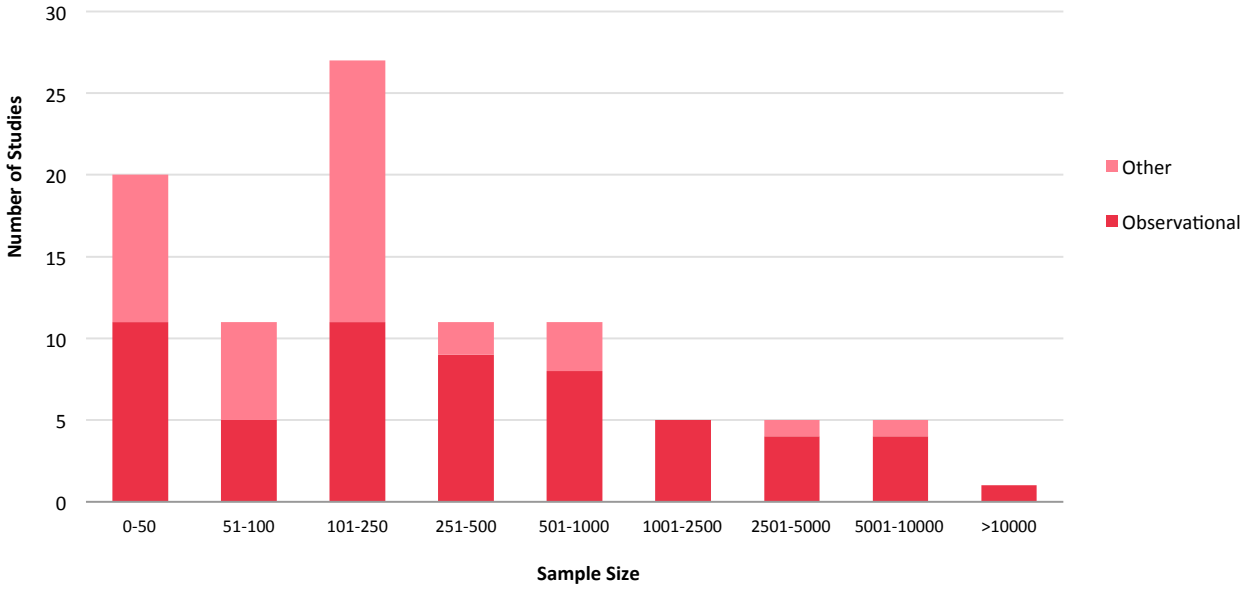
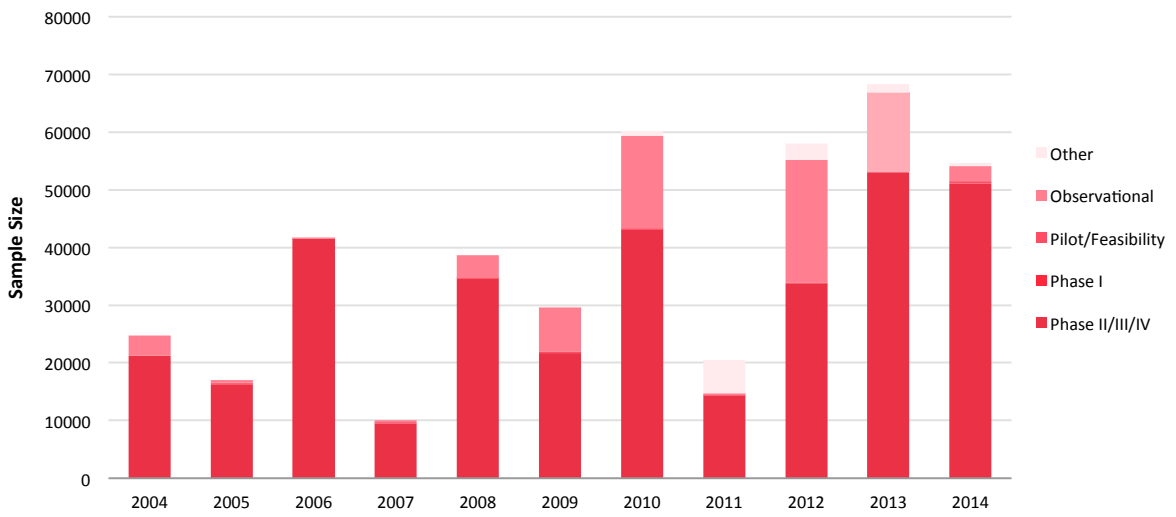


FIGURE 5-7: NUMBER OF COMPLETED PUBLISHED STUDIES BY SAMPLE SIZE –NON-INTERVENTIONAL STUDIES (N=93)



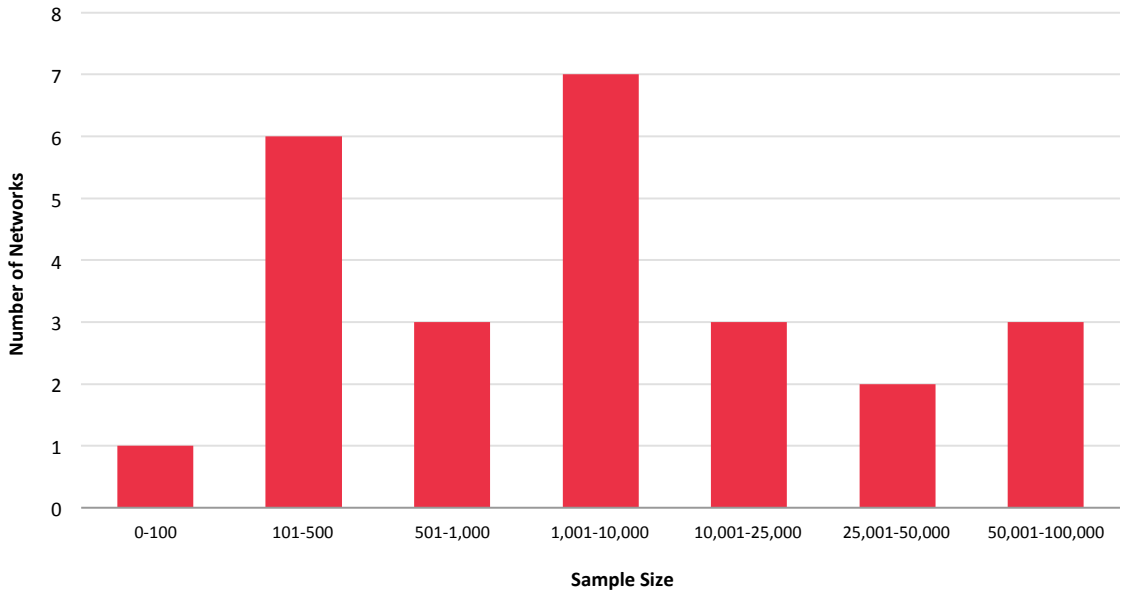
The aggregated sample sizes of studies published each year between 2004 and 2014 is displayed in Figure 5-8. The number of participants in studies published by networks in any one year ranged from 10,046 in 2007, to more than 60,000 in 2013. The majority of participants (n=340,153, 80%) were recruited into phase II, III and IV clinical trials, followed by observational studies (n=70,015, 7%) and the 'other' studies (n=11,718 2.7%). Only a very small proportion of the total number of participants reported were recruited into pilot/feasibility studies (n=1,362, 0.3%) and phase I clinical trials (n=195, 0.05%).

FIGURE 5-8: AGGREGATED SAMPLE SIZE OF COMPLETED PUBLISHED STUDIES PER YEAR (N=410)



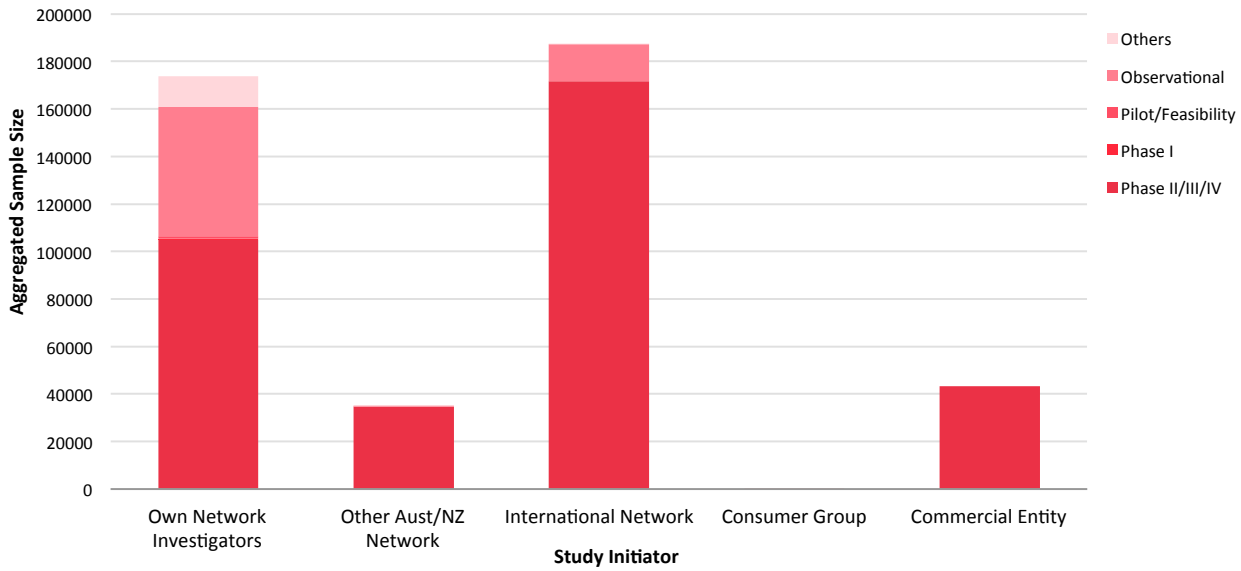
The distribution of recruited participants among networks that reported published studies is shown in Figure 5-9. The median (IQR) number of participants in studies completed and published per network was 2,825 (343 – 21,795) participants. Within the last 10 years, there were 17 networks with published studies that had recruited up to 10,000 participants, 3 networks with studies that had recruited between 10,001 and 25,000 participants, 2 networks with studies that had recruited between 25,001 and 50,000 participants and 3 networks with studies that had recruited between 50,001 and 100,000 participants.

FIGURE 5-9: AGGREGATED SAMPLE SIZE OF COMPLETED PUBLISHED STUDIES PER NETWORK (N=443)



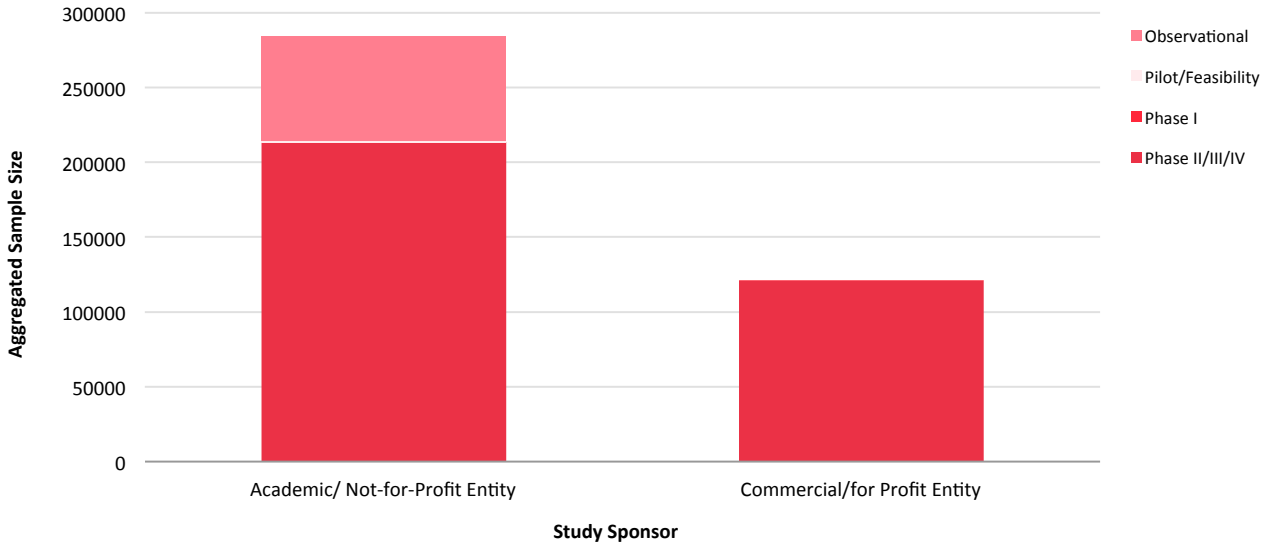
The aggregated sample size of completed published studies distributed according to study initiator is shown in Figure 5-10 and according to study sponsor is shown in Figure 5-11. The largest proportion of participants recruited into published studies came from studies initiated by an international network (n= 187,549, 43%), followed by studies initiated by the network's own investigators (n=173,855, 39%), studies initiated by a commercial entity (n=43,389, 10%), and studies initiated by another Australian/New Zealand network (n=35,175, 8% participants). Less than 1% (n=60) of the participants were involved in studies initiated by a consumer group.

FIGURE 5-10: AGGREGATED SAMPLE SIZE OF COMPLETED PUBLISHED STUDIES BY STUDY INITIATOR (N=439)



A total of 71% (n=297,766) of participants recruited by networks into published studies were involved in a study that was sponsored by an academic/not-for-profit entity, and 39% (n=120,974) were in a study that was commercially sponsored.

FIGURE 5-11: AGGREGATED SAMPLE SIZE OF COMPLETED PUBLISHED STUDIES BY TYPE OF STUDY SPONSOR (N=385)

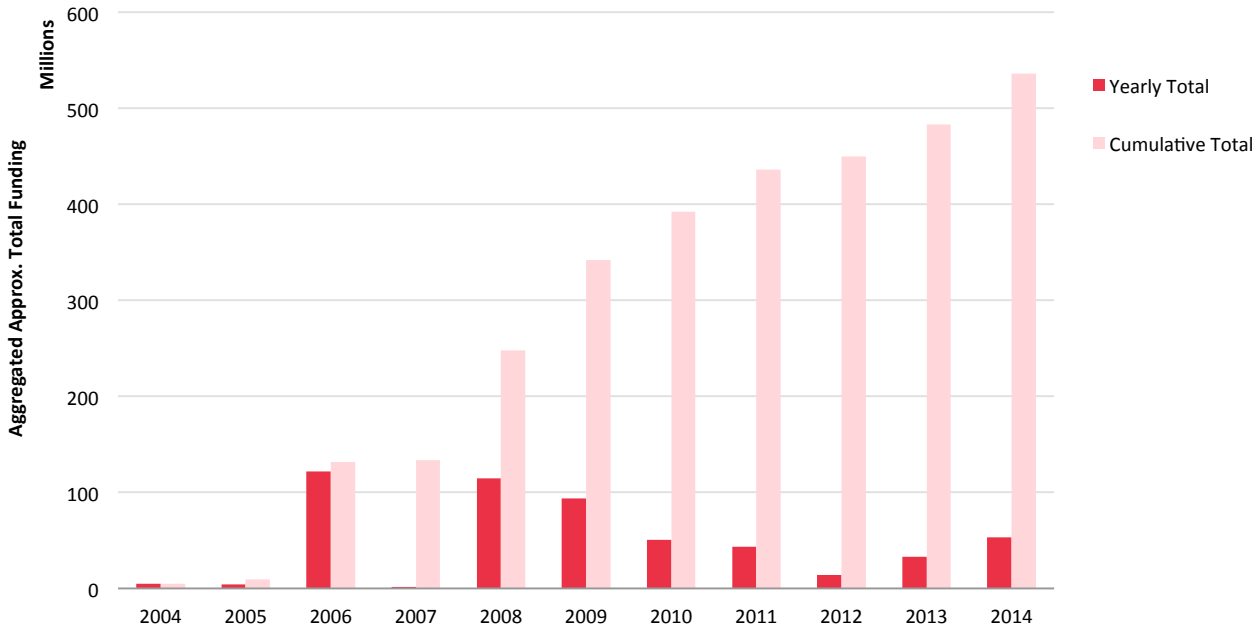


5.4 Funding of completed published studies

Estimated funding amounts were available for only around one third (n=160, 34%) of the published studies reported. These studies had an aggregate sample size of 180,072 participants, which corresponds to 43% of the total participant recruitment. Among the 160 studies for which estimated funding amounts were available, the approximate total funding (derived from all sources) that was reported for these studies was $536.2 M.

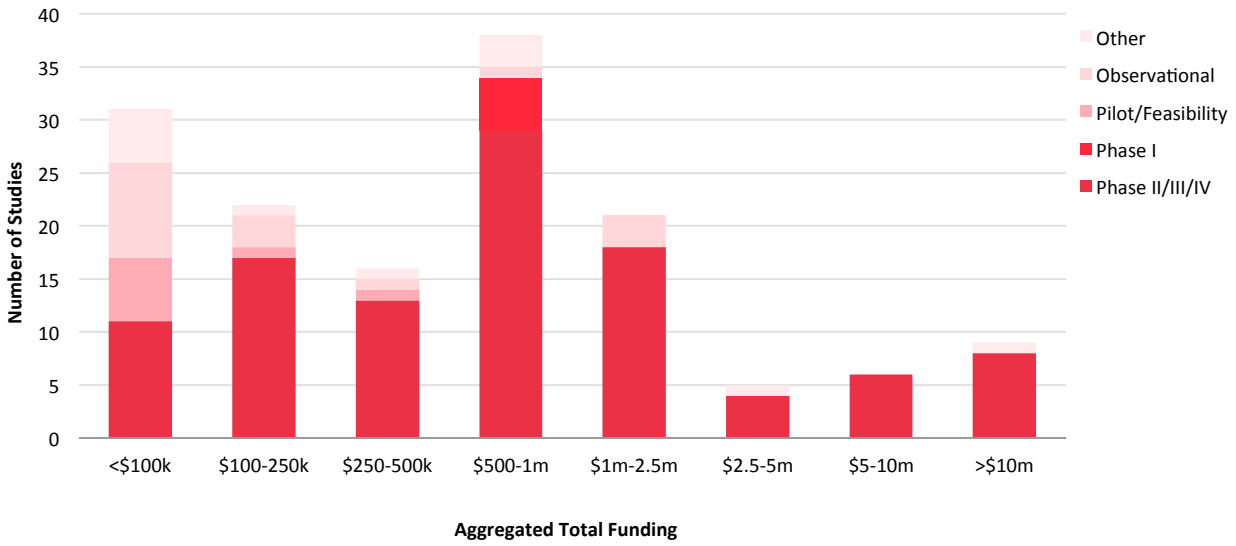
The annual (reported by year of publication) and cumulative estimated total funding for completed published studies is displayed in Figure 5-12. The reported estimated total funding amounts ranged from $0 - $100m per study, with a median (IQR) of $0.57m ($0.19m - $1.1m) per study. Among phase II/III/IV clinical trials only, and excluding the two $100m studies, the median (IQR) total funding per trial was $0.61m ($0.25m - $1.6m).

FIGURE 5-12: AGGREGATED TOTAL FUNDING OF COMPLETED PUBLISHED STUDIES PER YEAR (N=155)



The number of completed published studies corresponding to different ranges of aggregated total funding per study is shown in Figure 5-13. There were 31 studies with <$100k in total funding, 22 studies with between $100-250k, 15 studies with between $250-500k, 38 studies with between $500-1m, 21 studies with between $1m-2.5m (including 3 large observational studies), 4 studies with between $2.5-5m (including 1 basic science investigation), and 6 studies with between $5-10m in total funding.

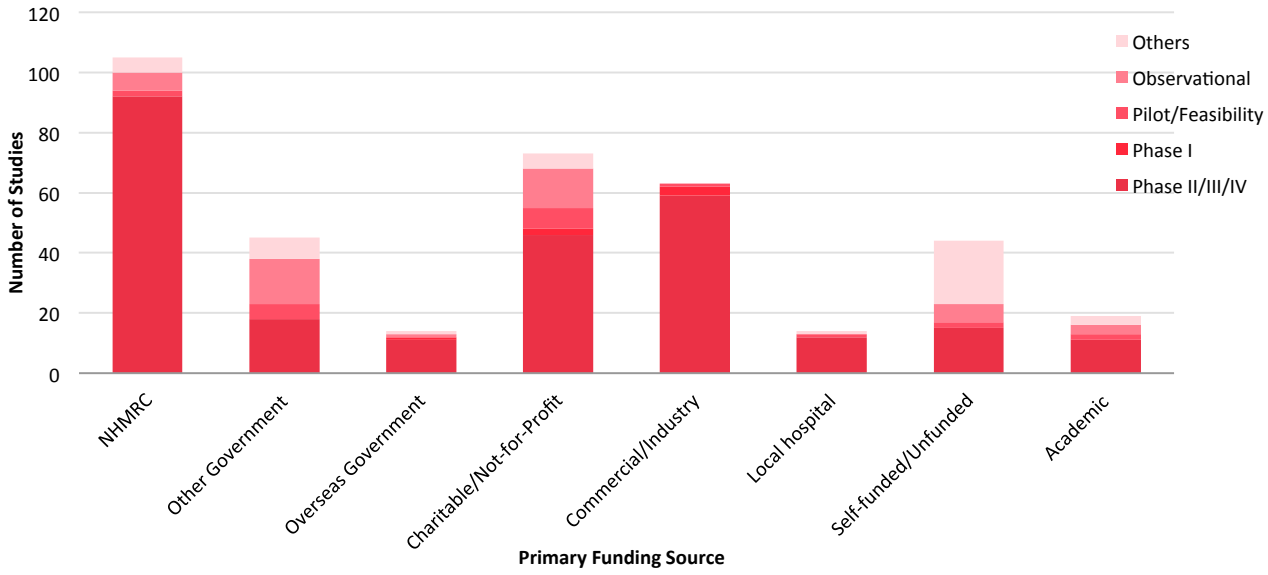
FIGURE 5-13: AGGREGATED TOTAL FUNDING FOR COMPLETED PUBLISHED STUDIES BY STUDY TYPE (N=148)



Networks were asked to identify the primary source of funding for each completed published study (defined as the funder contributing the greatest proportion of the approximate total funding amount). This information was available for 377 studies and the number of studies for each identified primary funding source is shown in Figure 5-14.

The NHMRC was the most frequently reported primary funding source (n=105, 28%), followed by charitable/philanthropic funding (n=73, 19%). There were also a substantial number of studies reported to be primarily self-funded by the network (n=44, 12%), by other Government sources (n=45, 12%) or academic sources (n=19, 5%). Only a small number of the studies (7%) were equally divided between overseas Governments (n=14) and local hospitals (n=14) as the primary funding source. A total of 63 studies (17%) were identified as having a commercial/for profit entity as the primary funder.

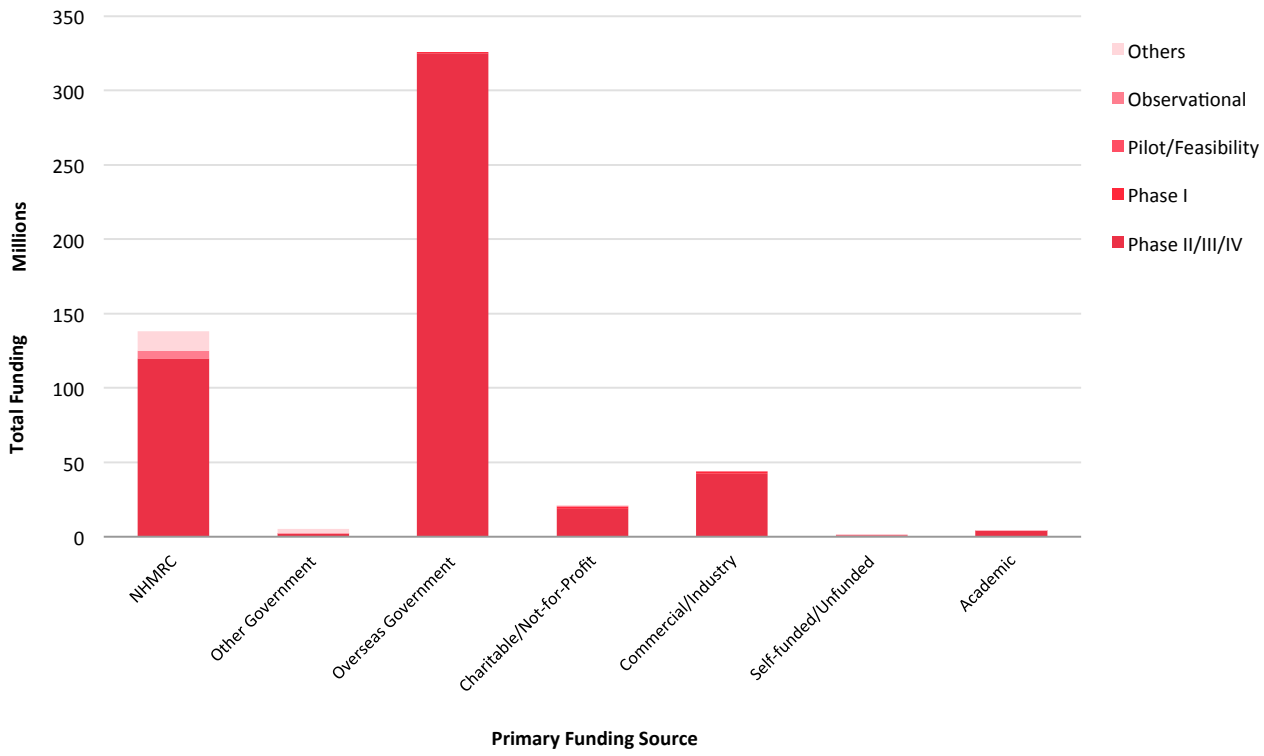
FIGURE 5-14: NUMBER OF COMPLETED PUBLISHED STUDIES BY PRIMARY FUNDING SOURCE (N= 377)



Information regarding the amount of funding from the primary funding source was available for 160 studies and is displayed in Figure 5-15. Offshore funding where an overseas government was the primary funder, contributed the largest amount of aggregated total funding for published studies ($325.8m, 60%) but a large component of this funding was $200m reported for two large international trials. Funding from the NHMRC accounted for the second highest amount of total funding ($138.1m, 26%).

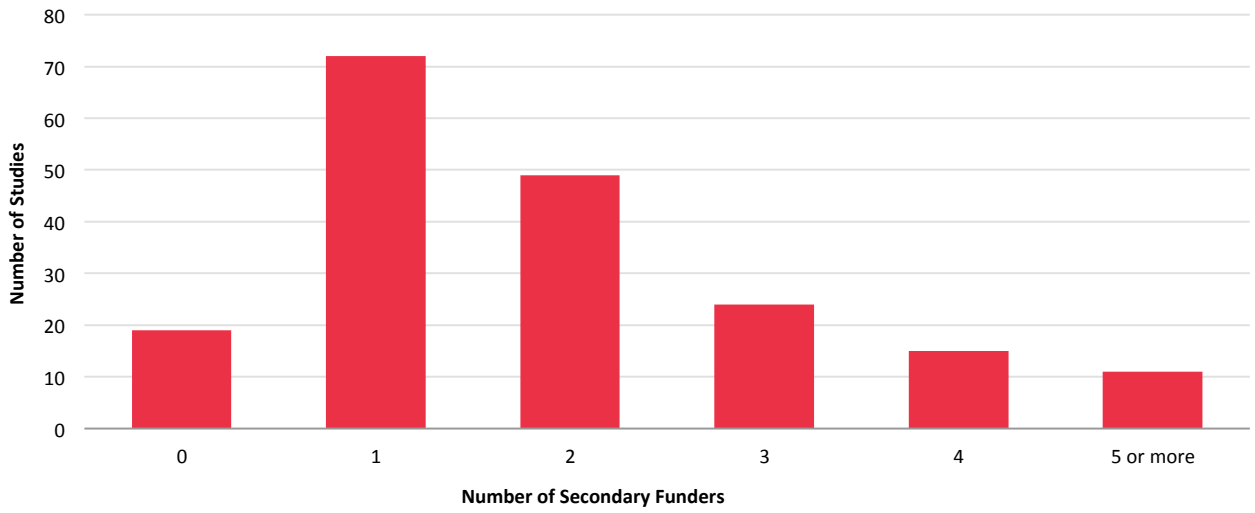
The remainder was distributed between commercial/for profit primary funders ($43.9m, 8%), charitable/not-for-profit primary funders (4%, $20.9m), and other Australian Government sources as primary funders ($5.2m, 1%). Only a small proportion was contributed by academic sources as the primary funder ($3.9m, 0.7%) and self-funded/unfunded studies ($1.2m, 0.3%).

FIGURE 5-15: AGGREGATED TOTAL FUNDING BY PRIMARY FUNDING SOURCE (N=160)



Where applicable, networks were also asked to identify the secondary funding sources for each study. The number of secondary funders identified per study is reported in Figure 5-16. These data were only available for 190 studies (41% of all 467 published studies). Among these studies there were: 19 (10%) studies with no secondary funders, 72 (38%) studies with 1 secondary funder, 49 (26%) studies with 2 secondary funders, 24 (13%) studies with 3 secondary funders, 15 (8%) studies with 4 secondary funders, and 11 (5%) studies with 5 or more secondary funders identified.

FIGURE 5-16: NUMBER OF SECONDARY FUNDING SOURCES FOR COMPLETED PUBLISHED STUDIES (N= 190)

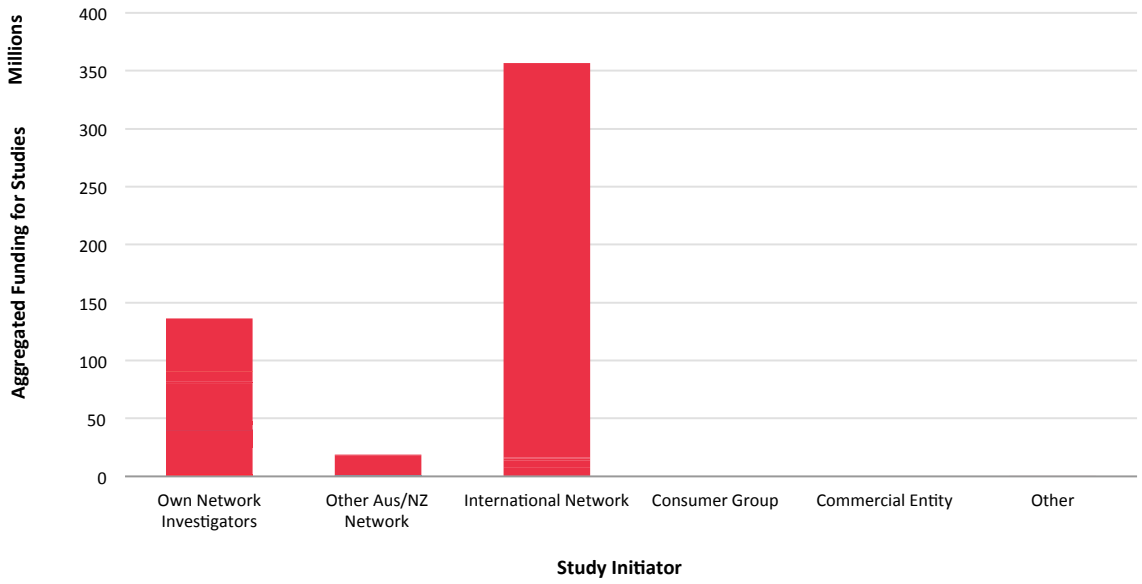


The amount of total funding for completed published studies that was contributed per network is reflected in Figure 5-17. There was median funding of $ 1.2m ($0.3m – $9.9m) per network. Furthermore, there were 3 networks that reported <$100k; 5 networks reported between $100k-1m, 4 networks that reported between $1-2.5m, 3 networks that reported between $5-10m, 1 network that reported between $10-25m, 1 network that reported between $25-50m, and 2 networks with an approximate total funding for completed studies that was >$50m.

FIGURE 5-17: AGGREGATED TOTAL FUNDING FOR COMPLETED PUBLISHED STUDIES PER NETWORK (N=148)

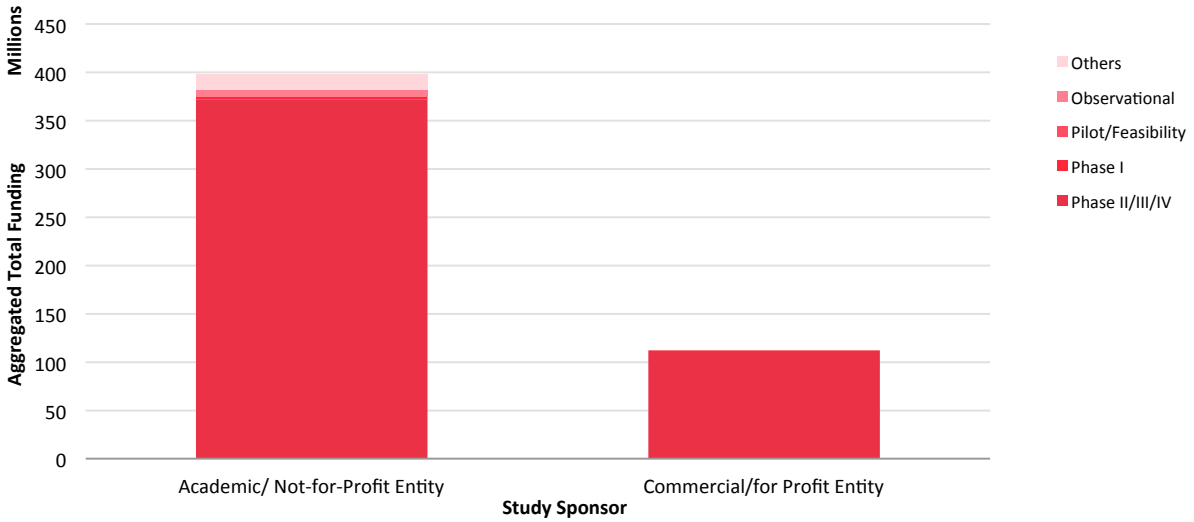
As shown in Figure 5-18, of the total funding identified for published studies where the study initiator was known, $356.8m (70%) was from studies initiated by an international network (including $200m associated with 2 large multinational trials), $136.4m (26%) came from studies that were initiated by the networks' own investigators, and $18.8m (4%) from studies initiated by another Australian network. There were no funding data available for published studies *initiated by* (as opposed to sponsored by) a commercial entity.

FIGURE 5-18: AGGREGATED TOTAL FUNDING FOR COMPLETED PUBLISHED STUDIES BY STUDY INITIATOR (N= 164)



Finally, Figure 5-19 shows that where the type of study sponsor was known, the vast majority of funding reported was for studies with an academic/not-for-profit sponsor, $397.9m (78%), as opposed to $112.4m (22%) for commercially sponsored studies.

FIGURE 5-19: AGGREGATED TOTAL FUNDING FOR COMPLETED PUBLISHED STUDIES BY STUDY SPONSOR (N=210)



5.5 Summary of key findings

- There were 26 Australian clinical trials networks that reported at least one completed study that was published between 2000 and 2014. These networks completed 467 different studies during the 10-year time period.
- The number of studies published by networks per year more than doubled between 2004 and 2014.
- Phase II/III/IV clinical trials were the most common study type comprising 69% of published studies. Networks undertake only minimal phase I trial activity.
- More than 420,000 participants were recruited into network studies - of which more than 340,000 were randomised within a clinical trial. There were 151 clinical trials conducted with a sample size of more than 250 participants.
- The vast majority of studies conducted by networks (95%) were investigated-initiated (as opposed to studies initiated by commercial entities) and more than half of these (58%) were designed and led by Australian investigators.
- More than 90% of studies had an academic (non-commercial) sponsor.
- At least $536.2 million of funding was generated for network studies. However, this is likely to be a substantial under-estimate of total funding as this was derived from only 34% of completed studies corresponding to 43% of total recruitment.

6

Snapshot of Studies Currently Being Undertaken by Australian Clinical Trials Networks

6 Snapshot of Studies Currently Being Undertaken by Australian Clinical Trials Networks

6.1 Notes on interpreting these results

For the purpose of this report, **Current Studies** refers to studies that have been commenced but had not yet been completed at the time of reporting or at 31 December 2014 (whichever came first). A study was regarded as commenced if it had received or had been awarded funding; and was regarded as not yet complete if the primary results manuscript had not yet been published. The progression of these studies was categorised as being one of the following:

- Funded and in development but recruitment not yet commenced
- Recruitment open
- Recruitment complete and in follow up
- Completed with the manuscript for the primary results in development
- Completed with the manuscript for the primary results submitted
- Terminated with cessation of recruitment without having achieved initial or adjusted sample size

Completeness of the data
As with published studies, each analysis was conducted using only the valid data available for that analysis (no assumptions were made for missing data). The number of valid records available to be analysed is described for each figure. The completeness of data varies substantially across different variables and this should be taken into account when interpreting the results as they are presented.

Number of studies
Of the current studies, there were 15 that were collaborations between 2 or more networks. During the data collection stage these studies were reported by all of the collaborating networks. Duplicated studies were identified and only included within the analysis as a single study (unless otherwise specified), taking into account that 2 or more networks were contributing to the study.

Target sample size
Networks were asked to report target sample size but different approaches were taken by some networks for studies that involved recruitment in Australia as well as overseas. Some networks reported only the target sample size for recruitment in Australia whereas for other studies the total sample size for the entire study was reported.

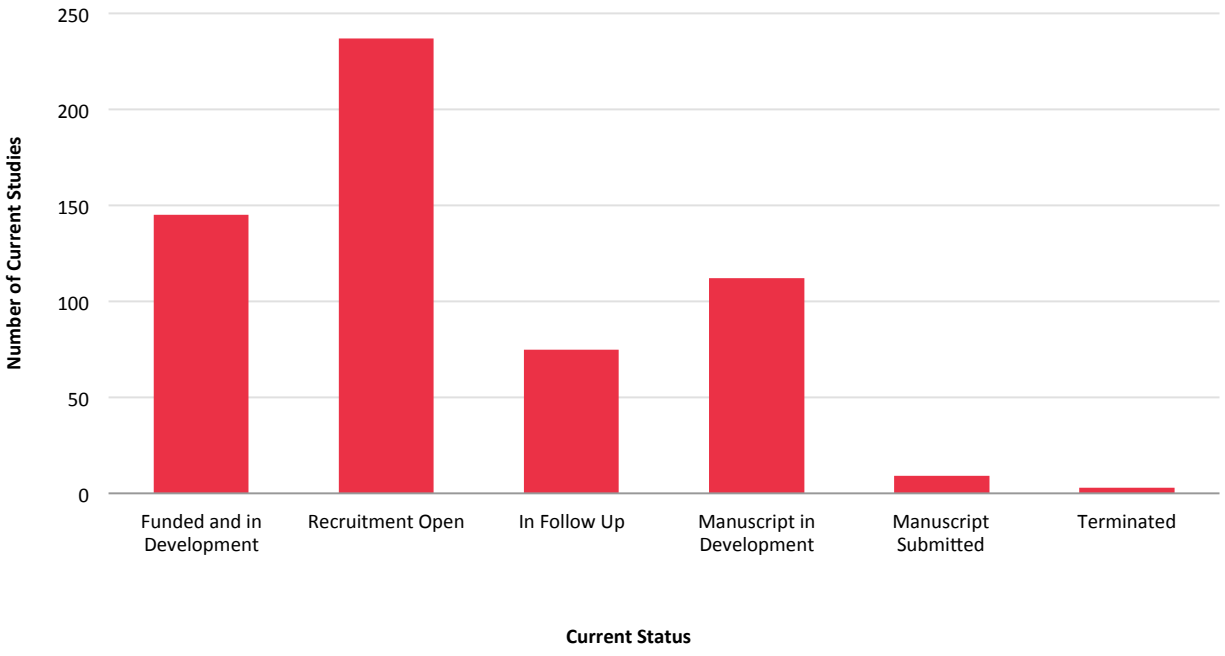
Approximate total funding
Networks were asked to provide an approximate figure for total amount of funding for each study but these data could only be obtained for around half (49%, 295 studies) of all of the current studies that were identified by networks. Consequently, funding figures are likely to substantially underrepresent the total amount of funding that has been generated by networks for current studies. Also of note is that there was a single large current international trial with a reported approximate total funding amount of $100 million that has been included in these analyses. This trial has been identified separately in some figures to provide clarity.

Networks were also asked to identify the primary funder for the study, and to list any secondary funders. Many studies received funding from multiple sources so the approximate total funding amount does not necessarily reflect the amount that received from the primary funding source.

6.2 Number of current studies

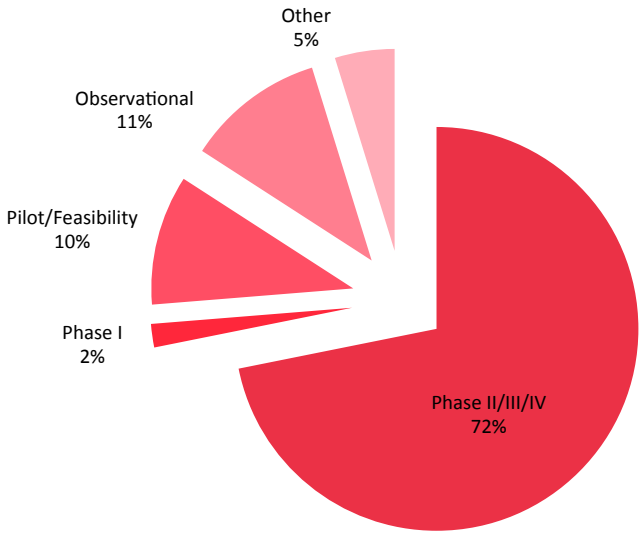
There were 588 current studies reported by participating networks. The current status reported for these studies is shown in Figure 6-1. There were 322 (55%) studies that were reported to be in the 'active phase' of data collection – either open to recruitment (n=237, 41%) or recruitment completed and in follow-up (n=75, 13%). There were 124 (21%) studies that had been completed but the primary results were not yet published. Of these, 115 (20%) had not yet submitted a manuscript for publication and 9 (2%) studies in which manuscripts had been submitted. Three studies (0.5%) were terminated without being completed. A further 147 (25%) studies were in the development pipeline; having received or awarded funding but had not yet commenced recruitment. Of note, there were a number of networks that reported having numerous additional studies they considered to be in advanced stages of development but for which funding had not yet been obtained.

FIGURE 6-1: NUMBER OF CURRENT STUDIES BY CURRENT STATUS (N= 581)



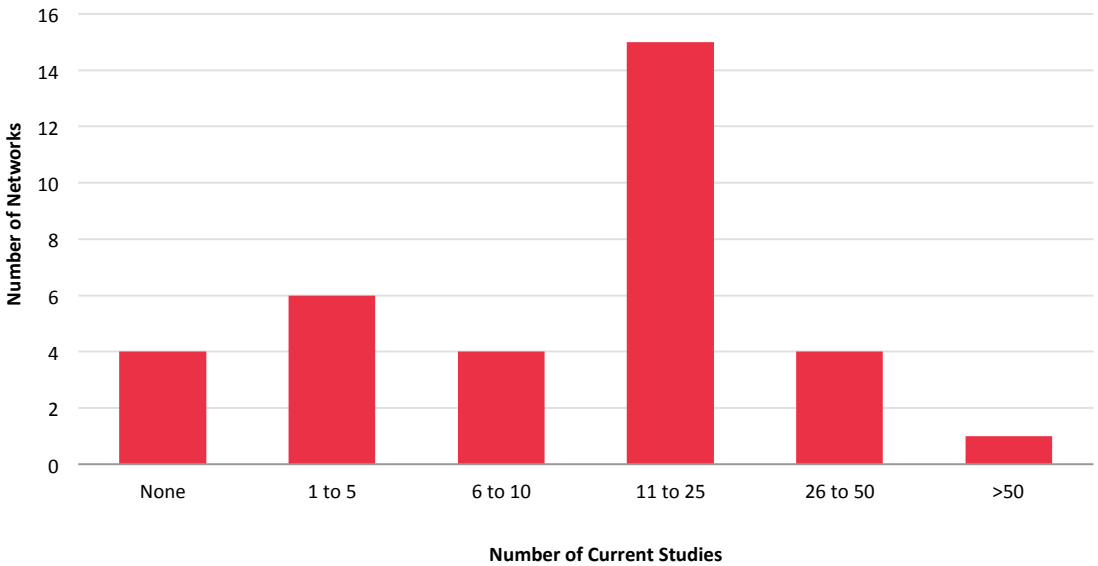
The proportion of different types of studies currently underway by networks is reflected in Figure 7-2. The vast majority of studies reported were identified as phase II, III or IV clinical trials (n=421, 72%), followed by observational studies (n=65, 11%) and pilot or feasibility studies (n=61, 10%). Only 11 studies (2%) were identified as phase I clinical trials. For 28 studies (5%) the study type was recorded as 'others' and included surveys, validations studies and retrospective audits.

FIGURE 6-2: NUMBER OF CURRENT STUDIES BY STUDY TYPE (N=586)



The distribution of current studies among networks is displayed in Figure 6-3. The number of current studies reported per network ranged from 0 to 149 studies with a median (IQR) of 12 (8 - 17) studies per network. There were 4 networks that had no studies currently underway; 10 networks with between 1 and 10 current studies; 15 networks with between 11 and 15 current studies; 4 networks with between 26 and 50 current studies and 1 network that reported having more than 50 current studies underway. It should be noted that collaborative studies involving more than one network are attributed to each participating network (i.e. reported more than once).

FIGURE 6-3: NUMBER OF CURRENT STUDIES PER NETWORK (N=603)

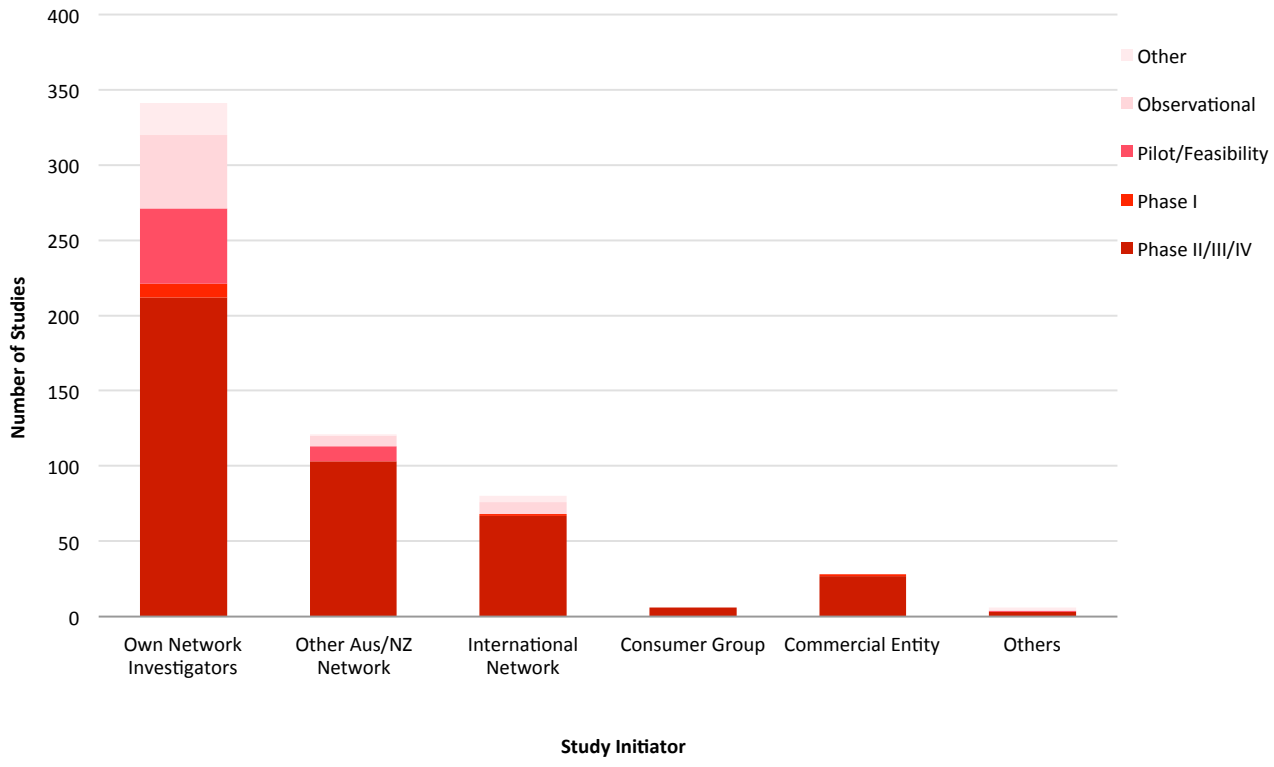


Networks were asked to identify the primary initiator of the study, classified as either:

- the network's own investigators;
- another Australian/New Zealand network;
- an international network;
- a consumer group;
- a commercial entity; or
- 'other'

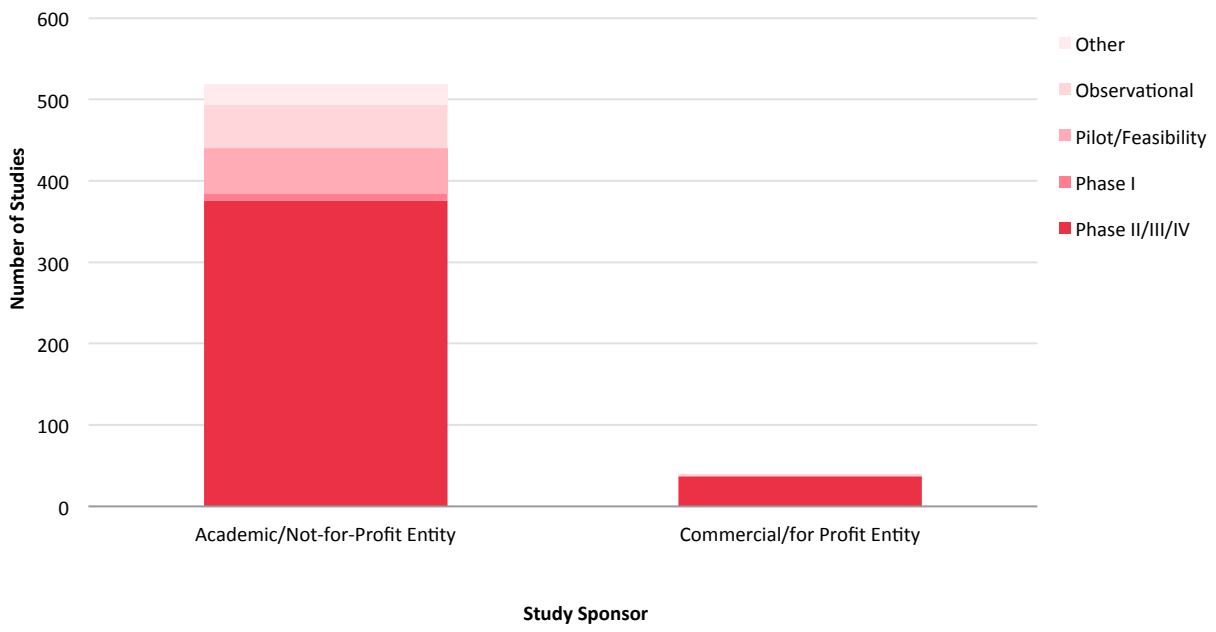
These results displayed in Figure 6-4 show that the vast majority of current studies were investigator-initiated (n=542, 93%). Of these, 341 (59%) studies had been initiated by the network's own investigators, 121 (21%) by another Australian or Australian and New Zealand network, and 80 (14%) by investigators from another international network. There were 28 studies (5%) that were initiated by a commercial or for profit entity. The remainder were initiated by a consumer group (n=6, 2%) or described as 'other' (n=6, 2%).

FIGURE 6-4: NUMBER OF CURRENT STUDIES BY STUDY INITIATOR (582)



Where the initiator of a study was known, the proportion of current studies with an academic or not-for-profit sponsor was 93% (n=519), with 7% (n=40) that were identified as having a commercial sponsor (see Figure 6-5).

FIGURE 6-5: NUMBER OF CURRENT STUDIES BY STUDY SPONSOR (N=559)

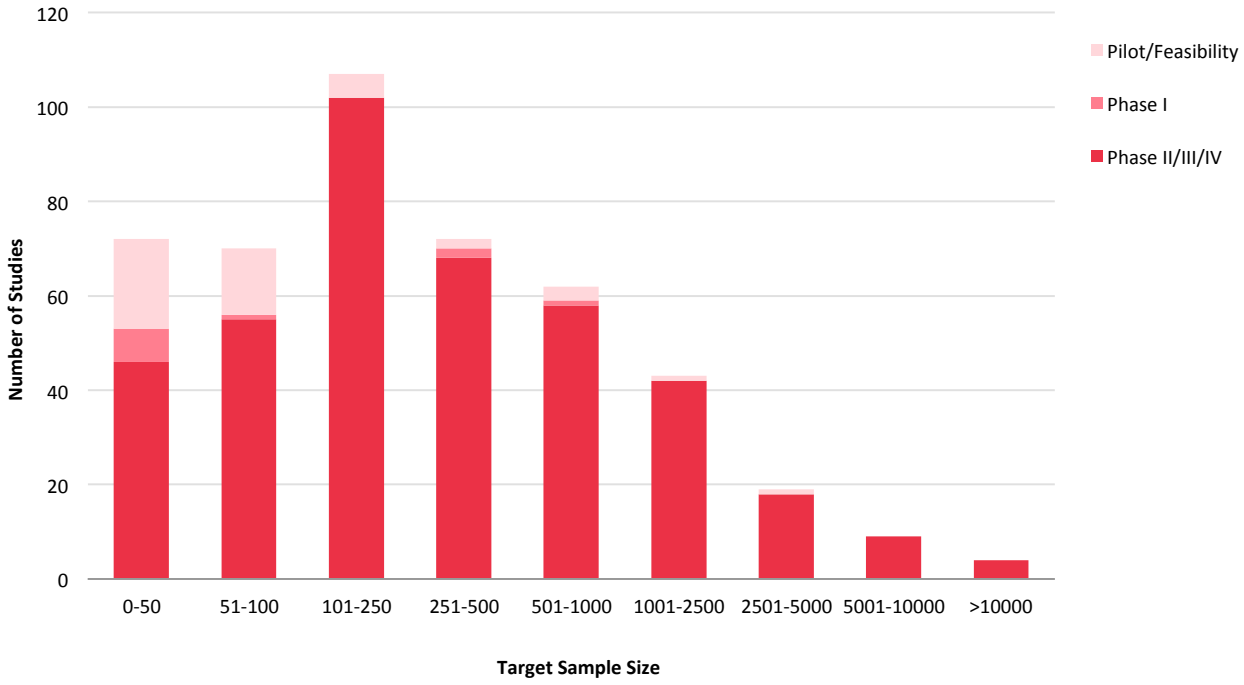


6.3 Target number of participants in current studies

The total reported target sample size aggregated across all current studies was 500,595 participants. The ranges of target sample sizes for current studies that were interventional studies (phase I-IV clinical trials or pilot/feasibility studies) or observational/other studies are shown in Figure 6-6 and Figure 6-7 respectively. Among the interventional clinical trials (n=458), the range of target sample sizes was 1 – 23,600 with a median (IQR) of 220 (100 – 673) participants per trial.

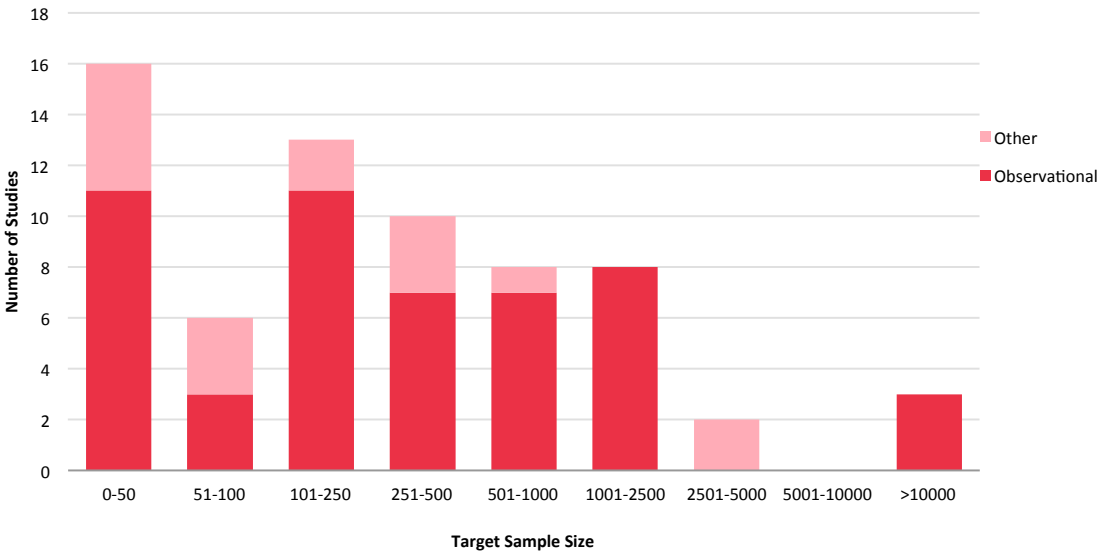
The target sample size was less than 250 participants for 249 trials, between 251 to 1000 participants for 134 trials, between 1,001 and 2,500 participants for 43 trials, between 2,501 and 5,000 participants for 19 trials, between 5,001 and 10,000 participants for 9 trials, and there were 4 trials that are aiming to recruit more than 10,000 participants.

FIGURE 6-6: NUMBER OF CURRENT STUDIES BY TARGET SAMPLE SIZE – INTERVENTIONAL STUDIES (N= 458)



There were also several large non-interventional studies underway across participating networks, including 8 studies that will involve between 1,001 and 2,500 participants, two studies that will involve between 2,501 and 5,000 participants and three observational studies that will each involve more than 10,000 participants. The combined total target sample size of these three studies alone was more than 50,000 participants.

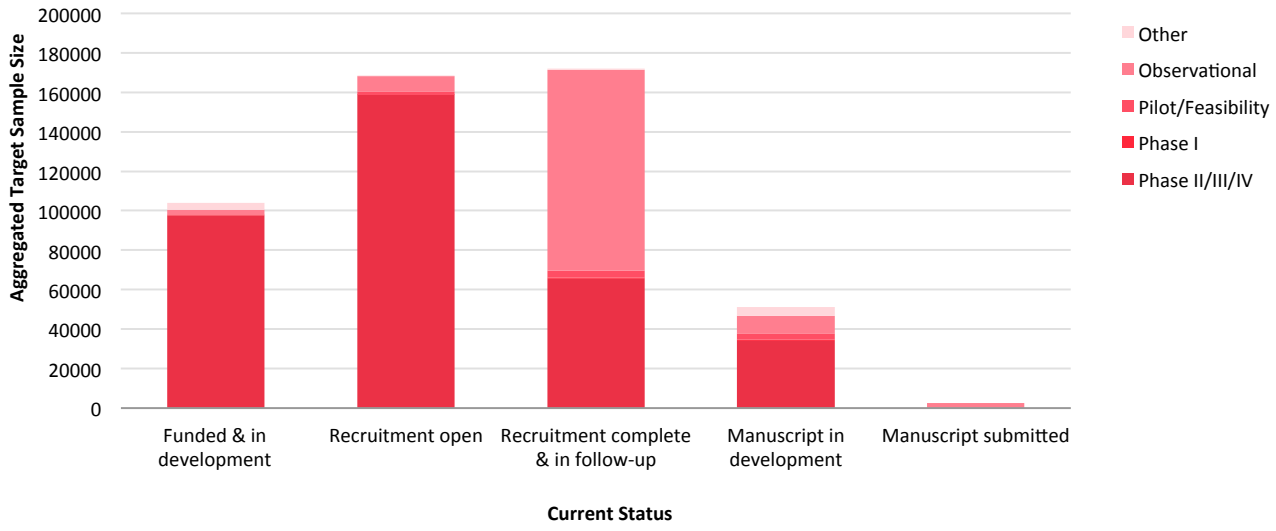
FIGURE 6-7: NUMBER OF CURRENT STUDIES BY TARGET SAMPLE SIZE – OBSERVATIONAL/OTHER STUDIES (N = 66)



The aggregated target sample sizes of current studies at different stages of study completion are displayed in Figure 6-8. There were a total of 500,002 planned participants reported across current studies that were either open to recruitment (n=168,514, 34%), in follow-up (n=171,955, 34%) or had been completed with the primary manuscript in development (n=51,295, 10%) or submitted for publication (n=2,420, 0.5%). Additionally, there was a strong pipeline of development evident, with studies that aim to recruit more 100,000 participants already funded and in development (n=105,818, 21%).

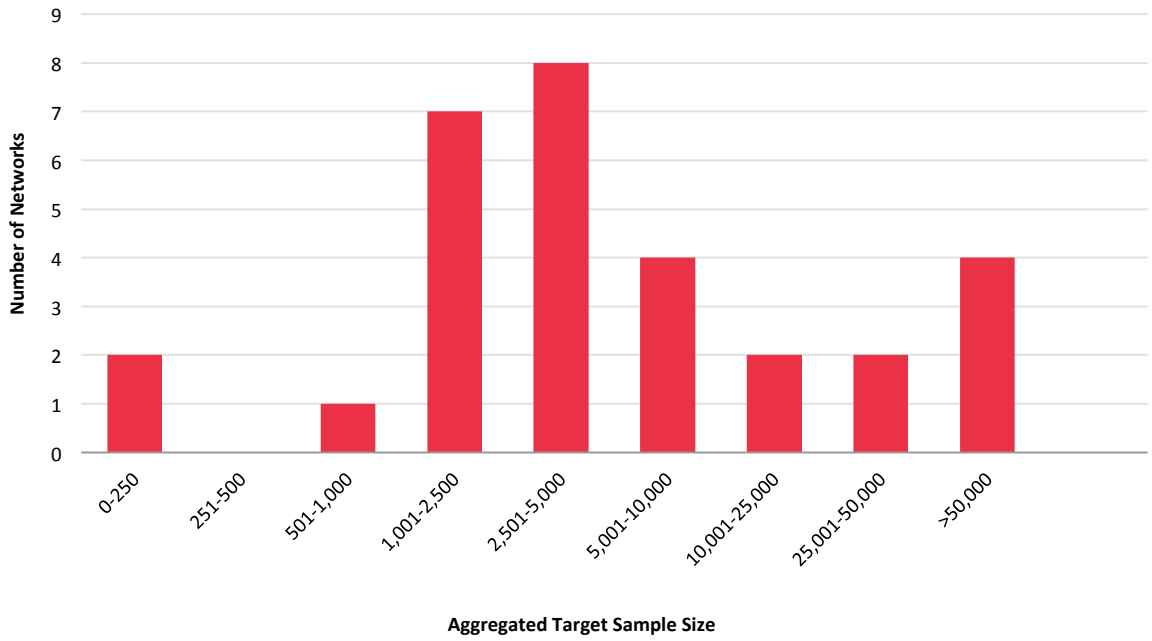
Once again, the majority of participants were identified for phase II, III and IV clinical trials (n=356,079, 71%). However, observational studies did account for a significant proportion – approximately 25% (n=122,877) of the aggregated target sample size of network studies currently underway. Pilot/Feasibility studies (n=9,971, 2%), studies classified as 'others' (n= 9,308, 2%) and phase I clinical trials (n=1,767, 0.4%) made up the remainder.

FIGURE 6-8: AGGREGATED TARGET SAMPLE SIZE OF CURRENT STUDIES BY STATUS (N=499)



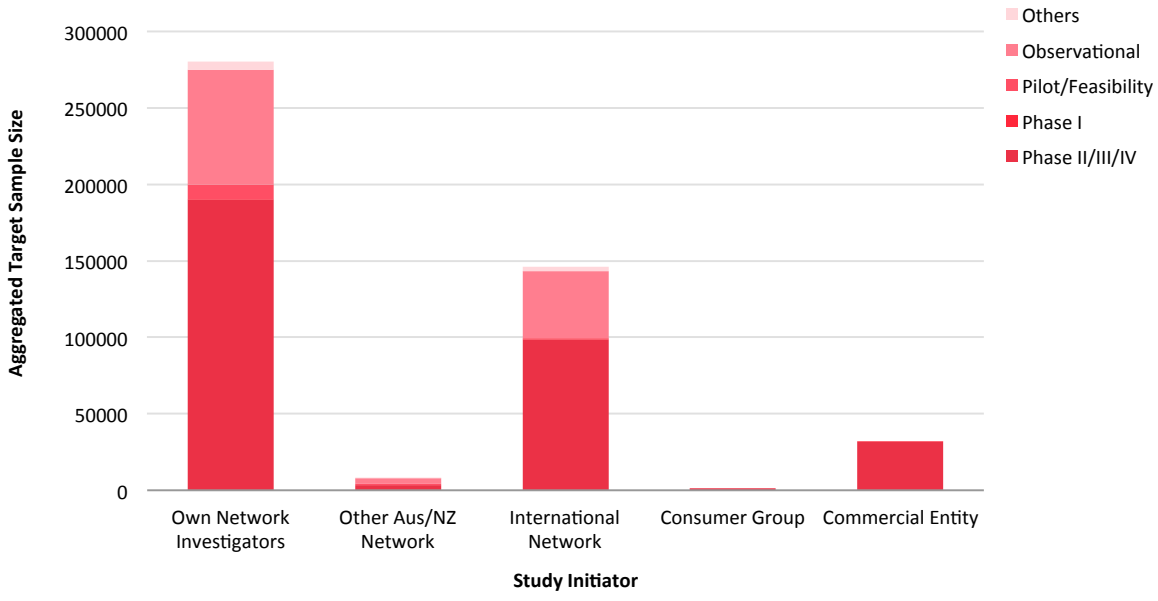
The distribution of the aggregated target sample size among networks that reported current studies is shown in Figure 6-9. The median total target sample size of all current studies per network was 3,694 (1,353 – 9,557) participants. There were 18 networks that reported current studies aiming to recruit a total of between 1 and 5,000 participants, 4 networks aiming to recruit between 5,001 and 10,000 participants, 2 networks aiming to recruit between 10,001 and 25,000 participants, 2 networks aiming to recruit between 25,001 and 50,000 participants, and 4 networks with current studies aiming to recruit more than 50,000 participants.

FIGURE 6-9: AGGREGATED TARGET SAMPLE SIZE OF CURRENT STUDIES PER NETWORK (N=525)



The aggregated sample size of current studies distributed according to study initiator is shown in Figure 6-10 and according to study sponsor is shown in Figure 6-11. The majority of participants that networks reported they were aiming to recruit into current studies were for studies initiated by the network's own investigators (n=280,246, 56%), followed by studies initiated by an international network (n=146,322, 29%), and studies initiated by another Australian or Australian and New Zealand network (n=38,410, 8%). Approximately 6% (n=32,224) of the aggregated target sample size was for studies initiated by a commercial entity and less than 1% (n=1443) for studies initiated by a consumer group.

FIGURE 6-10: AGGREGATED SAMPLE SIZE OF CURRENT STUDIES BY STUDY INITIATOR (N= 522)



A total of 90% (n=445,296) of participants that networks reported that they aim to recruit into current studies were in a study sponsored by an academic or not-for-profit entity and only 11% (n=48,095) were in a study with a commercial sponsor.

FIGURE 6-11: AGGREGATED SAMPLE SIZE OF CURRENT STUDIES BY TYPE OF STUDY SPONSOR (N=489)

6.4 Funding for current studies

The approximate total funding (all sources) reported for current studies, aggregate across all networks, was $475m. However, estimated funding amounts were available for only approximately half (n=295, 49%) of the studies for which the planned aggregate recruitment was 363,211 participants (corresponding to 73% of all planned recruitment). The estimated total funding amounts reported ranged from $0 - $100m per study, with a median (IQR) of $0.62m ($0.13m - $1.5m) per study. Among phase II, II and IV clinical trials only, and excluding the $100m study, the median (IQR) total funding per trial was $0.82m ($0.4m - $1.9m).

The breakdown of reported total funding for current studies in each stage of completion is shown in the Figure 6-12.

FIGURE 6-12: AGGREGATED TOTAL FUNDING OF CURRENT STUDIES BY STUDY STATUS (N= 295)

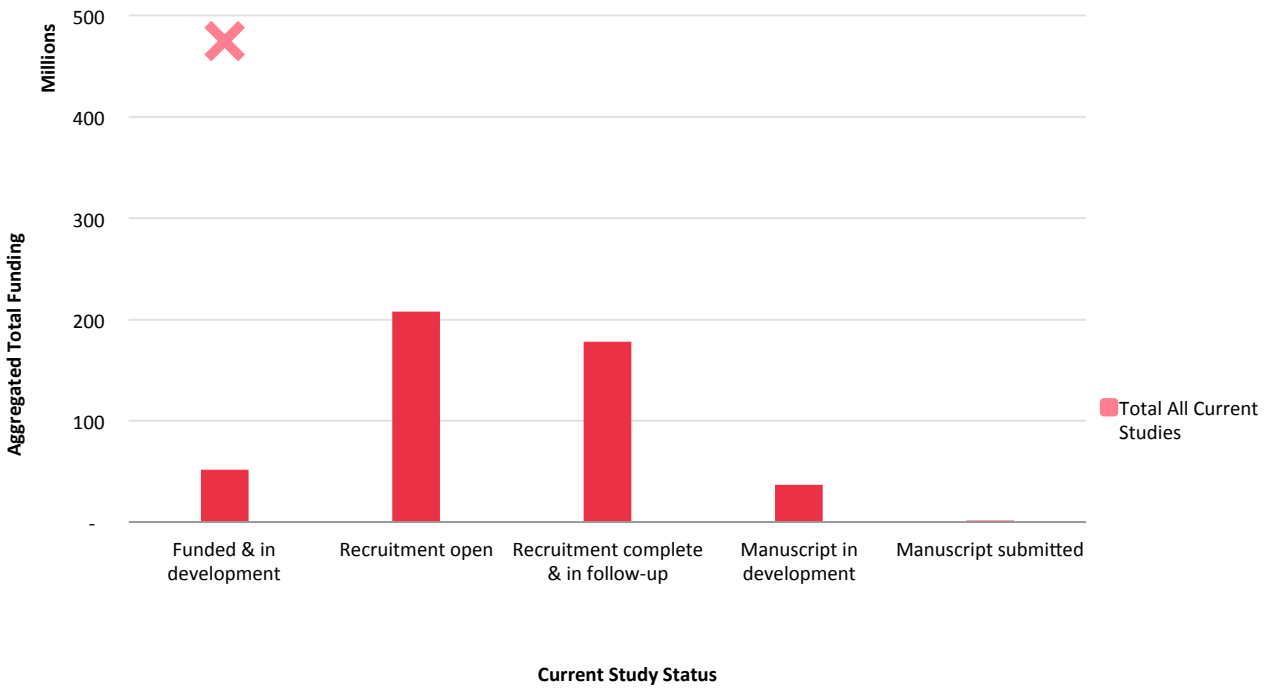
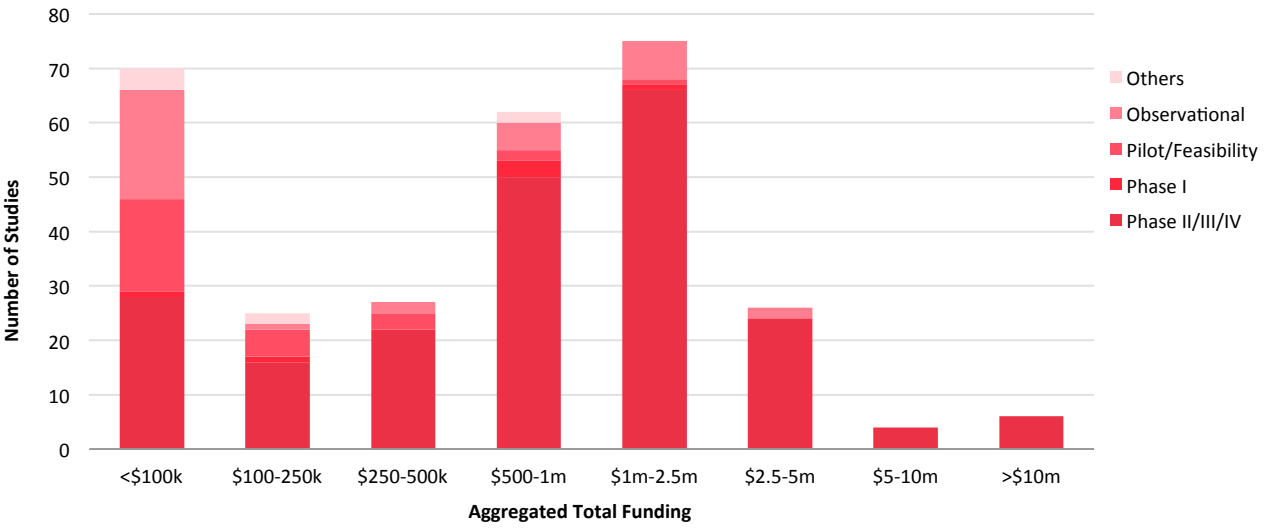


Figure 6-13 represents the number of current studies corresponding to different ranges of total funding. There were 70 studies with <$100k, 25 studies with between $100-250k in funding, 27 studies with between $250-500k, 62 studies with between $500k-1m, 75 studies with between $1m-2.5m (including 7 large observational studies), 26 studies with between $2.5-5m (including 2 large observational studies), 4 studies with between $5-10m, and 6 studies with more than $10m in total funding.

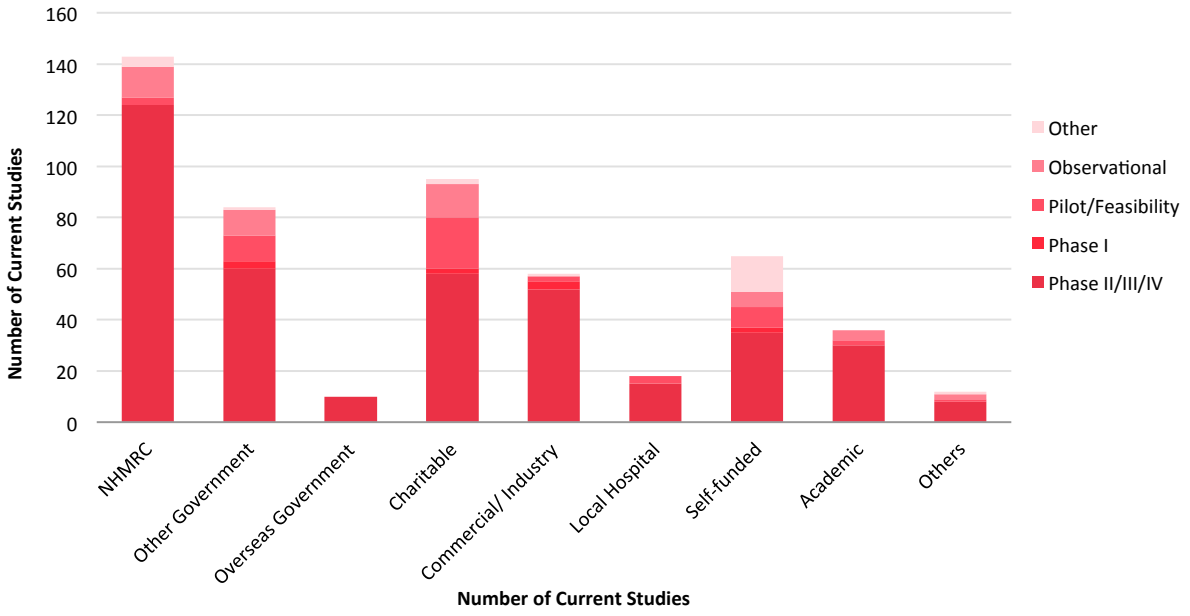
FIGURE 6-13: AGGREGATED TOTAL FUNDING FOR CURRENT STUDIES BY STUDY TYPE (N=295)



Networks were asked to identify the primary source of funding for each current study (defined as the funder contributing the greatest proportion of the approximate total funding per study). The numbers of studies per identified primary funding source, along with the amounts of funding derived from these sources, are shown in Figure 6-14 and Figure 6-15, respectively.

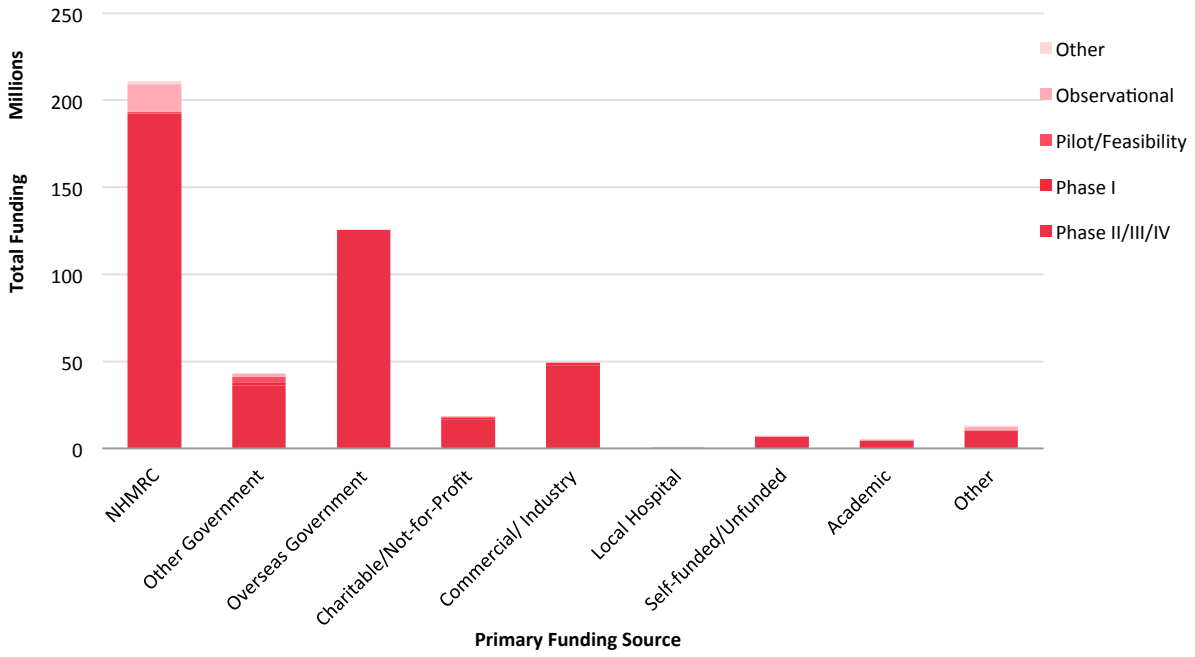
The NHMRC was the most frequently reported primary funding source (n=143, 27%), followed by charitable or philanthropic funding (n=95, 18%) and other Government sources (n=84, 16%). There were also a number of studies that were reported to be primarily self-funded by the network (n=65, 12%) and a smaller number reported to be primarily funded by an academic institution (n=36, 7%) or a local hospital (n=18, 3%). Only 2% (n=10) reported that an overseas Government was the primary funding source. A total of 58 studies (11%) were identified as having a commercial/for profit entity as the primary funder.

FIGURE 6-14: NUMBER OF CURRENT STUDIES BY PRIMARY FUNDING SOURCE (N=521)



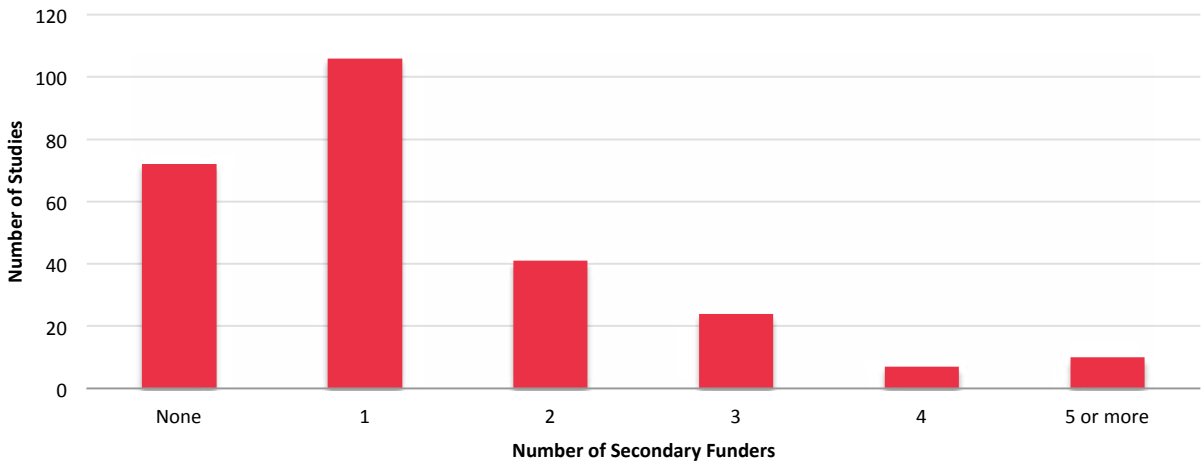
The NHMRC was also the primary funder that contributed the largest proportion of total funding reported for current studies ($211m, 46%). Offshore funding where an overseas government was the primary funder ($125.4m, 27%) was the second largest component, though this was largely due to a $100m amount reported for a single trial. Commercial or for profit entities were identified as the primary funder for 13% ($49.3m) of the total funding reported, followed by other Australian Government sources ($43.1m, 9%), charitable or not-for-profit entities ($18.4m, 4%), academic sources ($5.2m, 1%) and local hospitals ($0.06m, 0.01%). The networks themselves were identified as the primary funder for 1.5% ($6.9m) of the total funding for current studies reported.

FIGURE 6-15: AGGREGATED TOTAL FUNDING BY PRIMARY FUNDING SOURCE (N=295)



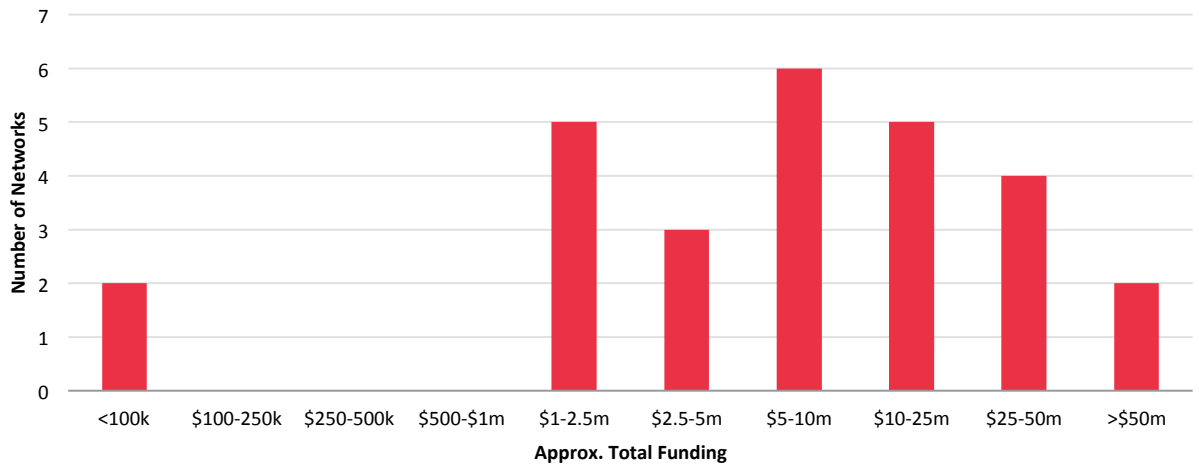
Where applicable, networks were also asked to identify the number of secondary funding sources for each study. The number of secondary funders identified per study is reported in Figure 6-16. These data were only available for 260 studies (44% of all current studies). Among these studies there were: 72 (28%) studies with no secondary funders, 106 (41%) studies with 1 secondary funder, 41 (16%) studies with 2 secondary funders, 24 (9%) studies with 3 secondary funders, 4 (2%) studies with 4 secondary funders and 10 (4%) studies with 5 or more secondary funders identified.

FIGURE 6-16: NUMBER OF SECONDARY FUNDING SOURCES FOR CURRENT STUDIES (N= 260)



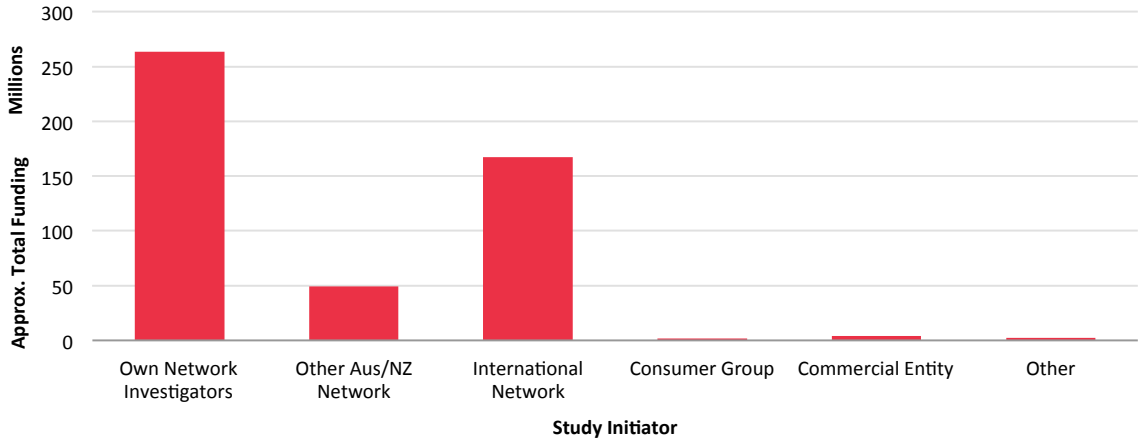
The amount of total funding for current studies that was contributed per network is reflected in Figure 6-17. There was a median (IQR) of $8.2m ($249k - $17.4m) per network. There were two networks that reported <$100k; 5 networks reported between $1-2.5m; three networks that reported between $2.5-5m, six networks that reported between $5-10m, five networks that reported between $10-25m, four networks that reported between $25-50m, and two networks with an approximate total funding for current studies that was >$50m.

FIGURE 6-17: AGGREGATED TOTAL FUNDING FOR CURRENT STUDIES PER NETWORK (N= 295)



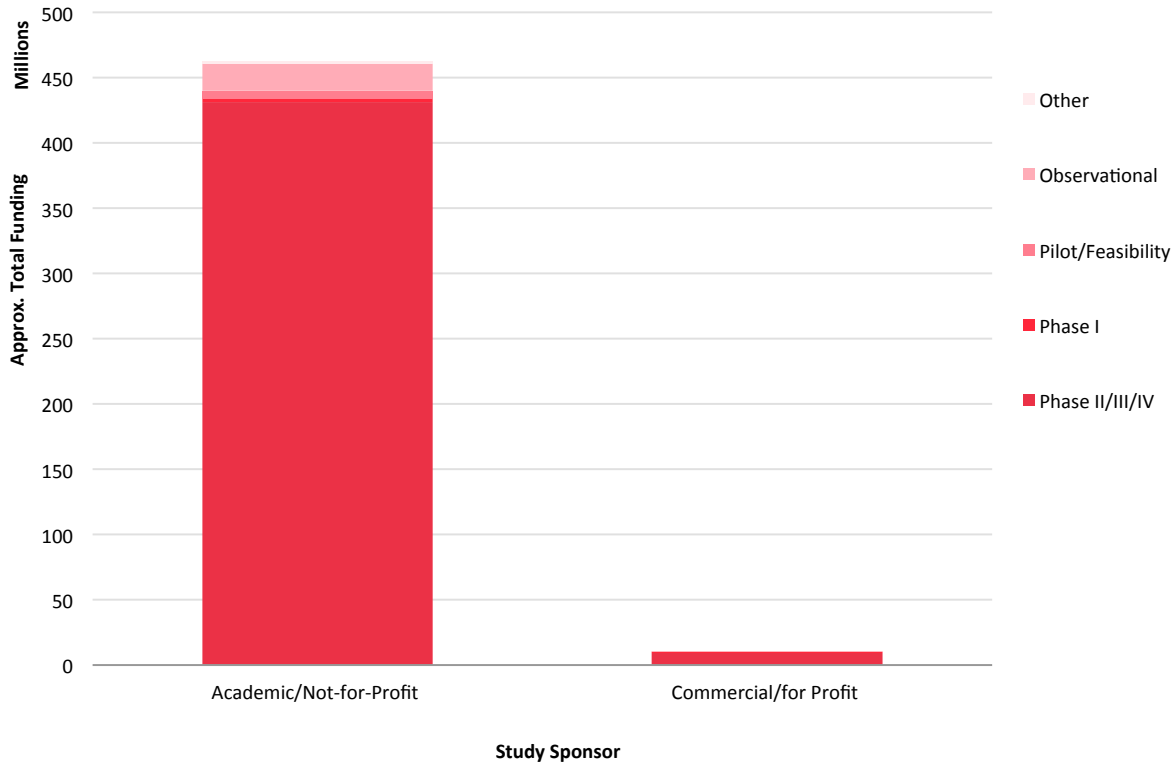
As shown in Figure 6-18, of the total amount of funding identified for current studies where the study initiator was known, $261.3m (55%) came from studies that were initiated by the network's own investigators, $167.3m (35%) from studies initiated by an international network (includes the single $100 multinational trial), $38.3m (8%) from studies initiated by another Australian or Australian and New Zealand network, and $1.6m (0.3%) from studies initiated by a consumer group. The total funding attributed to studies that were reported to be initiated by a commercial entity was only $3.9m (1%).

FIGURE 6-18: AGGREGATED TOTAL FUNDING FOR CURRENT STUDIES BY STUDY INITIATOR (N= 294)



Finally, Figure 6-19 shows that where the type of study sponsor was known, the vast majority of funding reported was for studies with an academic or not-for-profit sponsor ($466.8m, 98%) as opposed to $10m (2%) for commercially sponsored studies.

FIGURE 6-19: AGGREGATED TOTAL FUNDING FOR CURRENT STUDIES BY STUDY SPONSOR (N=292)



6.5 Summary of key findings

- There were 30 Australian clinical trials networks that reported one or more current studies.
- There were 588 different studies that are underway currently, of which 421 studies (72%) were phase II/III/IV clinical trials.
- The total planned sample size for current studies is more than 500,000 participants of which 356,000 participants have been or will be recruited into phase II/III/IV clinical trials. Among the half million participants, 225,000 have already been recruited into studies that have completed recruitment.
- The funding being used to support these studies is at least $475 million, but this is likely to be a significant under-estimate as this funding figure was derived from only around half of all studies though corresponding to around three quarters of all planned recruitment for current studies.
- The NHMRC was the source of more than $210 million of funding for current network studies. The NHMRC was responsible for primary funding of 27% of current studies, but these studies represent 46% of the amount of the total amount of funding (56% of total funding if a $100m study funded overseas is excluded).
- The vast majority of current network studies reported (93%) were investigator-initiated and more than half (59%) were led by Australian investigators. Almost all studies (98%) were sponsored by an academic or not-for-profit entity.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7

Impact of Studies Conducted by Australian Clinical Trials Networks

7 Impact of Studies Conducted by Australian Clinical Trials Networks

7.1 Reported impact on clinical practice and healthcare policy

Participating networks were asked to indicate whether a published study had, or was expected to have, a major impact on clinical practice, healthcare policy or both (policy/practice). It is important to note that a valid response was available to be analysed for less than one third of the total number of completed published studies (145/467 studies). Therefore, the number of network studies that have impacted on policy/practice reported here is likely to be a substantial underestimate.

There were 18 networks that reported a total of 98 studies with demonstrable impacts or results that were anticipated to result in impacts on policy/practice that had been published in the last 10 years. The majority of studies with reported impact were phase II, III, or IV clinical trials (n=85). Networks also reported 10 observational and three studies categories as "other" that had an impact on policy/practice. A response of "no impact" was recorded for 30 studies, and "not applicable" for 17 studies - the majority of which were Pilot/Feasibility studies.

Figure 7-1 shows the number of studies reported to have impacted policy/practice by year of publication of the primary study results and Figure 7-2 shows the distribution of these studies by network. The median (IQR) of studies with reported impact on policy/practice per year was 8 (7-10) studies. The majority of networks that reported these data had published between 1 and 5 studies with impact (n=12). There were four networks that reported 10 or more studies with impact. The median (IQR) number of published studies with reported impact on policy/practice per network was 3.5 [1-8.5] studies.

FIGURE 7-1: NUMBER OF STUDIES WITH REPORTED IMPACT ON PRACTICE/POLICY BY YEAR OF PUBLICATION (N=98).

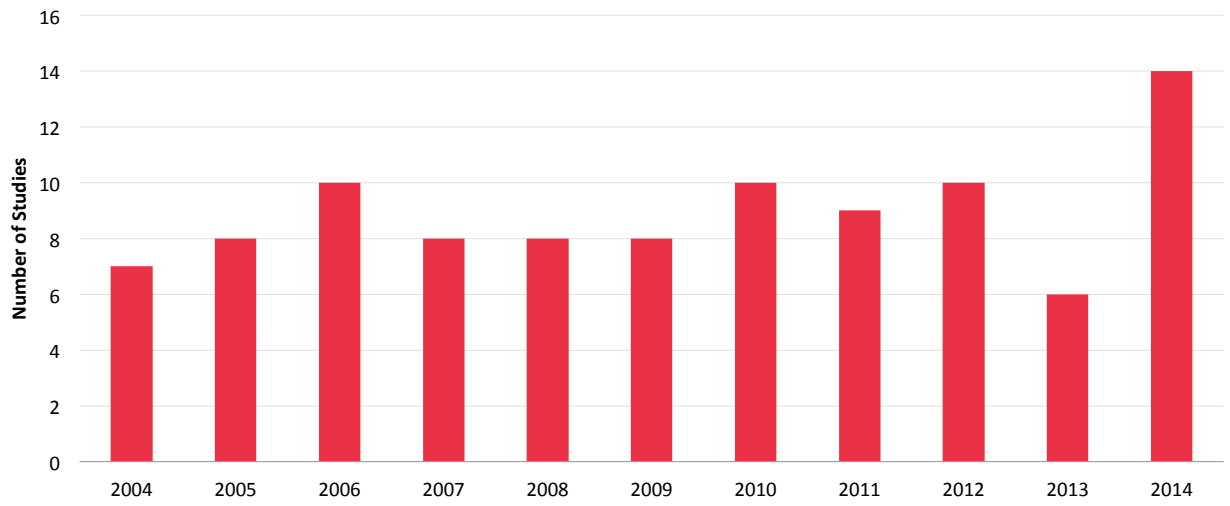
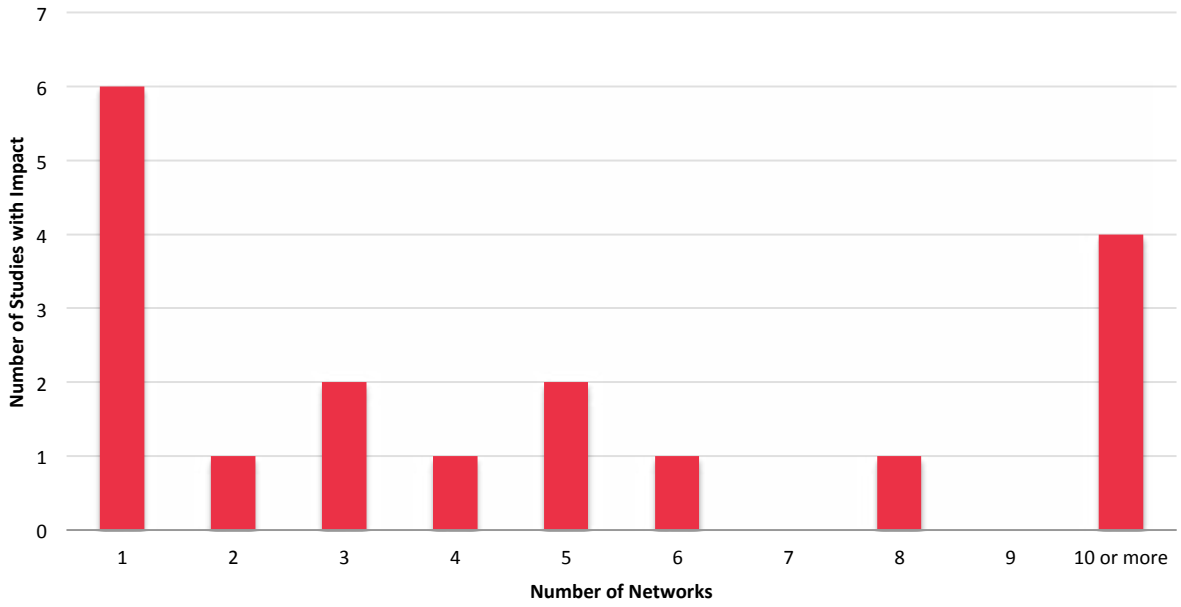


FIGURE 7-2: NUMBER OF COMPLETED PUBLISHED STUDIES WITH REPORTED IMPACT ON POLICY/PRACTICE BY NETWORK (N=98)



7.1.1 Examples of high-impact clinical trials conducted by Australian networks

Networks were also asked to provide a brief description of how the study has changed (or is expected to change) clinical practice/policy leading to improved healthcare outcomes or health system productivity. Of the 98 studies that reported impact, a brief description of impact was provided for 91 of these studies.

A selection of examples of high-impact clinical trials that were reported to have changed practice and/or policy in Australia - or in many cases, globally - is provided in Table 7-1**.** This table also includes some studies that were published in high impact general medical journals (section 7.3) but were not identified as having had an impact by the reporting network but were considered likely to have done so. It should be noted that although all of the trials contained within Table 7-1 are examples of Australia's world-class clinical trials expertise across a range of clinical areas, there are many other high-impact trials that have been conducted by networks that are not described in this table.

TABLE 7-1: EXAMPLES OF CLINICAL TRIALS REPORTED TO HAVE HAD AN IMPACT ON HEALTHCARE PRACTICE/POLICY

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
A Randomised Trial of Preoperative Radiotherapy for Stage T3 Adenocarcinoma of Rectum	TROG / AGITG	2012	326	Three hundred twenty-six patients were randomly assigned; 163 patients to SC [Short-Course Radiotherapy] and 163 to LC [Long-Course Radiotherapy]. Median potential follow-up time was 5.9 years (range, 3.0 to 7.8 years). Three-year LR [local recurrence] rates (cumulative incidence) were 7.5% for SC and 4.4% for LC (difference, 3.1%; 95% CI, -2.1 to 8.3; P = .24). For distal tumors (< 5 cm), six of 48 SC patients and one of 31 LC patients experienced local recurrence (P = .21). Five-year distant recurrence rates were 27% for SC and 30% for LC (log-rank P = 0.92; hazard ratio [HR] for LC:SC, 1.04; 95% CI, 0.69 to 1.56). Overall survival rates at 5 years were 74% for SC and 70% for LC (log-rank P = 0.62; HR, 1.12; 95% CI, 0.76 to 1.67). Late toxicity rates were not substantially different (Radiation Therapy Oncology Group/European Organisation for Research and Treatment of Cancer G3-4: SC, 5.8%; LC, 8.2%; P = .53). J Clin Oncol. 2012 Nov 1;30(31):3827-33 (5)	Three-year LR rates between SC and LC were not statistically significantly different; the CI for the difference is consistent with either no clinically important difference or differences in favour of LC. LC may be more effective in reducing LR for distal tumours. No differences in rates of distant recurrence, relapse-free survival, overall survival, or late toxicity were detected.	**"Added important information on short versus long course radiotherapy and gave clinicians information to guide therapy choice based on information about patient outcomes."**
A Randomised Trial Investigating the Effectiveness of Different Durations of Maximal Androgen Deprivation Prior to and During Definitive Radiation Therapy for Locally Advanced Carcinoma of the Prostate	TROG	2005	818	802 (98%) patients were eligible for analysis. Median follow-up was 5.9 years (range 0.1-8.5). Compared with patients assigned no androgen deprivation, those assigned 3 months' treatment had significantly improved local failure (hazard ratio [HR] 0.56 [95% CI 0.39-0.79], p=0.001), biochemical failure-free survival (0.70 [0.56-0.88], p=0.002), disease-free survival (0.65 [0.52-0.80], p=0.0001), and freedom from salvage treatment (0.73 [0.56-0.96], p=0.025). 6 months' androgen deprivation significantly improved local failure (0.42 [0.28-0.62], p<0.0001), biochemical failure-free survival (0.58 [0.46-0.74], p<0.0001), disease-free survival (0.56 [0.45-0.69], p<0.0001), freedom from salvage treatment (0.53 [0.40-0.71], p<0.0001), distant failure (0.67 [0.45-0.99], p=0.046) and prostate-cancer-specific survival (0.56 [0.32-0.98], p=0.04) compared with no androgen deprivation. Lancet Oncol. 2005 Nov;6(11):841-50 (6)	6 months' androgen deprivation given before and during radiotherapy improves the outlook of patients with locally advanced prostate cancer. Further follow-up is needed to estimate precisely the size of survival benefits. Increased radiation doses and additional periods of androgen deprivation might lead to further benefit.	**"TROG 96.01 showed that the chances of cancer returning in the prostate could be reduced by approximately 60% using hormone therapy prior to radiotherapy"**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
A Large, Simple Trial Comparing Two Strategies for Management of Anti-Retroviral Therapy (The SMART Study). A Comparison of Two Ways to Manage Anti-HIV Treatment (The SMART Study)	KIRBY TVRP	2006	5,472	A total of 5472 participants (2720 assigned to drug conservation and 2752 to viral suppression) were followed for an average of 16 months before the protocol was modified for the drug conservation group. At baseline, the median and nadir CD4+ counts were 597 per cubic millimeter and 250 per cubic millimeter, respectively, and 71.7% of participants had plasma HIV RNA levels of 400 copies or less per milliliter. Opportunistic disease or death from any cause occurred in 120 participants (3.3 events per 100 person-years) in the drug conservation group and 47 participants (1.3 per 100 person-years) in the viral suppression group (hazard ratio for the drug conservation group vs. the viral suppression group, 2.6; 95% confidence interval [CI], 1.9 to 3.7; P<0.001). Hazard ratios for death from any cause and for major cardiovascular, renal, and hepatic disease were 1.8 (95% CI, 1.2 to 2.9; P=0.007) and 1.7 (95% CI, 1.1 to 2.5; P=0.009), respectively. Adjustment for the latest CD4+ count and HIV RNA level (as time-updated covariates) reduced the hazard ratio for the primary end point from 2.6 to 1.5 (95% CI, 1.0 to 2.1). N Engl J Med 2006; 355:2283-2296 (7)	Episodic antiretroviral therapy guided by the CD4+ count, as used in our study, significantly increased the risk of opportunistic disease or death from any cause, as compared with continuous antiretroviral therapy, largely as a consequence of lowering the CD4+ cell count and increasing the viral load. Episodic antiretroviral therapy does not reduce the risk of adverse events that have been associated with antiretroviral therapy.	**"Changed HIV treatment guidelines globally and set future research directions"**
Effects of continuity of care by a primary midwife (caseload midwifery) on caesarean section rates in women of low obstetric risk: the COSMOS randomised controlled trial	IMPACT	2012	2,314	In total 2314 women were randomised-1156 to caseload and 1158 to standard care. Women allocated to caseload were less likely to have a caesarean section (19.4% versus 24.9%; risk ratio [RR] 0.78; 95% CI 0.67-0.91; P = 0.001); more likely to have a spontaneous vaginal birth (63.0% versus 55.7%; RR 1.13; 95% CI 1.06-1.21; P < 0.001); less likely to have epidural analgesia (30.5% versus 34.6%; RR 0.88; 95% CI 0.79-0.996; P = 0.04) and less likely to have an episiotomy (23.1% versus 29.4%; RR 0.79; 95% CI 0.67-0.92; P = 0.003). Infants of women allocated to caseload were less likely to be admitted to special or neonatal intensive care (4.0% versus 6.4%; RR 0.63; 95% CI 0.44-0.90; P = 0.01). No infant outcomes favoured standard care. BJOG. 2012 Nov;119(12):1483-92 (8)	In settings with a relatively high baseline caesarean section rate, caseload midwifery for women at low obstetric risk in early pregnancy shows promise for reducing caesarean births.	**"Annual cost saving in Australia based on 80% implementation of the intervention = $33.5 million"**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
Australian collaborative trial of supplements (ACTS) with vitamin C and E for the prevention of pre-eclampsia	IMPACT	2006	1,877	Of the 1877 women enrolled in the study, 935 were randomly assigned to the vitamin group and 942 to the placebo group. Baseline characteristics of the two groups were similar. There were no significant differences between the vitamin and placebo groups in the risk of preeclampsia (6.0 percent and 5.0 percent, respectively; relative risk, 1.20; 95 percent confidence interval, 0.82 to 1.75), death or serious outcomes in the infant (9.5 percent and 12.1 percent; relative risk, 0.79; 95 percent confidence interval, 0.61 to 1.02), or having an infant with a birth weight below the 10th percentile for gestational age (8.7 percent and 9.9 percent; relative risk, 0.87; 95 percent confidence interval, 0.66 to 1.16). N Engl J Med 2006; 354:1796-1806 (9)	Supplementation with vitamins C and E during pregnancy does not reduce the risk of preeclampsia in nulliparous women, the risk of intrauterine growth restriction, or the risk of death or other serious outcomes in their infants.	**"The trial showed conclusively that vitamin C and E do not prevent pre-eclampsia, which has influenced international practice and policy (e.g. WHO guidelines)"**
International Neonatal Immunotherapy Study	IMPACT	2011	3,502	There was no significant between-group difference in the rates of the primary outcome [the rate of death or major disability at the age of 2 years, with adjustment for gestational age], which occurred in 686 of 1759 infants (39.0%) who received intravenous immune globulin and in 677 of 1734 infants (39.0%) who received placebo (relative risk, 1.00; 95% confidence interval, 0.92 to 1.08). Similarly, there were no significant differences in the rates of secondary outcomes, including the incidence of subsequent sepsis episodes. In follow-up of 2-year-old infants, there were no significant differences in the rates of major or non-major disability or of adverse events. N Engl J Med. 2011 Sep 29;365(13):1201-11 (10)	Therapy with intravenous immune globulin had no effect on the outcomes of suspected or proven neonatal sepsis.	**"Intravenous immune globulin conclusively shown to have no effect on suspected or proven neonatal sepsis, therefore it was no longer recommended or used in Australia or globally resulting in substantial cost savings"**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
Comparison of carotid endarterectomy with PTA [percutaneous transluminal angioplasty] and medical Mx [management] in stroke/TIA [transient ischaemic attack] Pts [patients] with carotid or vertebral artery stenosis	ASTN	2009	505	Severe carotid restenosis (>or=70%) or occlusion occurred significantly more often in patients in the endovascular arm than in patients in the endarterectomy arm (adjusted hazard ratio [HR] 3.17, 95% CI 1.89-5.32; p<0.0001). The estimated 5-year incidence of restenosis was 30.7% in the endovascular arm and 10.5% in the endarterectomy arm. Patients in the endovascular arm who were treated with a stent (n=50) had a significantly lower risk of developing restenosis of 70% or greater compared with those treated with balloon angioplasty alone (n=145; HR 0.43, 0.19-0.97; p=0.04). Current smoking or a history of smoking was a predictor of restenosis of 70% or more (2.32, 1.19-4.54; p=0.01) and the early finding of moderate stenosis (50-69%) up to 60 days after treatment was associated with the risk of progression to restenosis of 70% or more (3.76, 1.88-7.52; p=0.0002). The composite endpoint of ipsilateral non-perioperative stroke or transient ischaemic attack occurred more often in patients in whom restenosis of 70% or more was diagnosed in the first year after treatment compared with patients without restenosis of 70% or more (5-year incidence 23%vs 11%; HR 2.18, 1.04-4.54; p=0.04), but the increase in ipsilateral stroke alone was not significant (10%vs 5%; 1.67, 0.54-5.11). Lancet Neurol. 2009 Oct;8(10):908-17 (11)	Restenosis is about three times more common after endovascular treatment than after endarterectomy and is associated with recurrent ipsilateral cerebrovascular symptoms; however, the risk of recurrent ipsilateral stroke is low. Further data are required from on-going trials of stenting versus endarterectomy to ascertain whether long-term ultrasound follow-up is necessary after carotid revascularisation.	**"Major shift in care with changed guidelines, that moved to recommending stenting"**
A Multi-Centre, Open Label Randomized Stratified Controlled Trial of the Effects of Blood Glucose Management on 90-Day All-Cause Mortality in a Heterogenous Population of Intensive Care Unit (ICU) Patients (NICE-SUGAR Study).	ANZICS CTG	2012	6,030	Of the 6104 patients who underwent randomization, 3054 were assigned to undergo intensive control and 3050 to undergo conventional control; data with regard to the primary outcome at day 90 were available for 3010 and 3012 patients, respectively. The two groups had similar characteristics at baseline. A total of 829 patients (27.5%) in the intensive-control group and 751 (24.9%) in the conventional-control group died (odds ratio for intensive control, 1.14; 95% confidence interval, 1.02 to 1.28; P=0.02). The treatment effect did not differ significantly between operative (surgical) patients and nonoperative (medical) patients (odds ratio for death in the intensive-control group, 1.31 and 1.07, respectively; P=0.10). Severe hypoglycemia (blood glucose level, ≤40 mg per deciliter [2.2 mmol per liter]) was reported in 206 of 3016 patients (6.8%) in the intensive-control group and 15 of 3014 (0.5%) in the conventional-control group (P<0.001). There was no significant difference between the two treatment groups in the median number of days in the ICU (P=0.84) or hospital (P=0.86) or the median number of days of mechanical ventilation (P=0.56) or renal-replacement therapy (P=0.39). N Engl J Med 2009; 360:1283-1297 (12)	In this large, international, randomized trial, we found that intensive glucose control increased mortality among adults in the ICU: a blood glucose target of 180 mg or less per deciliter resulted in lower mortality than did a target of 81 to 108 mg per deciliter.	**"Reversed international practice, changed major sets of international guidelines, saved countless lives"**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
A multi-centre prospective randomised trial of early decompressive craniectomy in patients with severe traumatic brain injury (DECRA Study)	ANZICS CTG	2011	155	Patients in the craniectomy group, as compared with those in the standard-care group, had less time with intracranial pressures above the treatment threshold (P<0.001), fewer interventions for increased intracranial pressure (P<0.02 for all comparisons), and fewer days in the intensive care unit (ICU) (P<0.001). However, patients undergoing craniectomy had worse scores on the Extended Glasgow Outcome Scale than those receiving standard care (odds ratio for a worse score in the craniectomy group, 1.84; 95% confidence interval [CI], 1.05 to 3.24; P=0.03) and a greater risk of an unfavorable outcome (odds ratio, 2.21; 95% CI, 1.14 to 4.26; P=0.02). Rates of death at 6 months were similar in the craniectomy group (19%) and the standard-care group (18%). N Engl J Med 2011; 364:1493-1502 (13)	In adults with severe diffuse traumatic brain injury and refractory intracranial hypertension, early bifrontotemporoparietal decompressive craniectomy decreased intracranial pressure and the length of stay in the ICU but was associated with more unfavorable outcomes.	**"An unexpected result that led to major change in clinical practice to avoid routine use of decompressive craniectomy which had previously been standard care"**
Multi-national, Randomized, Phase III, GCIG [Gynecologic Cancer InterGroup] Intergroup Study Comparing Pegylated Liposomal Doxorubicin (CAELYX) and Carboplatin vs. Paclitaxel and Carboplatin in Patients With Epithelial Ovarian Cancer in Late Relapse – The CALYPSO Trial	ANZGOG	2012	976	A total of 976 patients were randomised (467 to CD [carboplatin-pegylated liposomal doxorubicin (PLD)] and 509 to CP [carboplatin-paclitaxel]). With a median follow-up of 49 months, no statistically significant difference was observed between arms in OS [overall survival] (hazard ratio = 0.99 (95% confidence interval 0.85, 1.16); log-rank P = 0.94). Median survival times were 30.7 months (CD) and 33.0 months (CP). No statistically significant difference in OS was observed between arms in predetermined subgroups according to age, body mass index, treatment-free interval, measurable disease, number of lines of prior chemotherapy, or performance status. Post-study cross-over was imbalanced between arms, with a greater proportion of patients randomised to CP receiving post-study PLD (68%) than patients randomised to CD receiving post-study paclitaxel (43%; P < 0.001). Br J Cancer. 2012 Aug 7;107(4):588-91 (14)	Carboplatin-PLD led to delayed progression and similar OS compared with carboplatin-paclitaxel in platinum-sensitive ROC [recurrent ovarian cancer].	**"'Changed the standard of care for platinum sensitive recurrent ovarian cancer in that carboplatin and caelyx shown to be more effective and much better tolerated than carboplatin and taxol"**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
An International Collaborative Trial for Relapsed and Refractory Acute Lymphoblastic Leukaemia.	ANZCHOG	2011	120	This open-label randomised trial was undertaken in 22 centres in the UK and Ireland and nine in Australia and New Zealand. Patients aged 1–18 years with first relapse of acute lymphoblastic leukaemia were stratified into high-risk, intermediate-risk, and standard-risk groups on the basis of duration of first complete remission, site of relapse, and immunophenotype. All patients were allocated to receive either idarubicin or mitoxantrone in induction by stratified concealed randomisation. Neither patients nor those giving interventions were masked. After three blocks of therapy, all high-risk group patients and those from the intermediate group with post-induction high minimal residual disease (≥10−4 cells) received an allogenic stem-cell transplant. Standard-risk and intermediate-risk patients with post-induction low minimal residual disease (<10−4 cells) continued chemotherapy. The primary outcome was progression-free survival and the method of analysis was intention-to-treat. Randomisation was stopped in December, 2007 because of differences in progression-free and overall survival between the two groups. Lancet. 2010 Dec 11; 376(9757):2009–2017 (15)	As compared with idarubicin, mitoxantrone conferred a significant benefit in progression-free and overall survival in children with relapsed acute lymphobastic leukaemia, a potentially useful clinical finding that warrants further investigation.	**"Changed international practice by removing the use of an inferior induction drug for children with leukaemia"**
Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial.	ANZCA CTN	2008	8,351	All 8351 patients were included in analyses; 8331 (99.8%) patients completed the 30-day follow-up. Fewer patients in the metoprolol group than in the placebo group reached the primary endpoint (244 [5.8%] patients in the metoprolol group vs 290 [6.9%] in the placebo group; hazard ratio 0.84, 95% CI 0.70-0.99; p=0.0399). Fewer patients in the metoprolol group than in the placebo group had a myocardial infarction (176 [4.2%] vs 239 [5.7%] patients; 0.73, 0.60-0.89; p=0.0017). However, there were more deaths in the metoprolol group than in the placebo group (129 [3.1%] vs 97 [2.3%] patients; 1.33, 1.03-1.74; p=0.0317). More patients in the metoprolol group than in the placebo group had a stroke (41 [1.0%] vs 19 [0.5%] patients; 2.17, 1.26-3.74; p=0.0053). Lancet. 2008 May 31; 371(9627):1839-47 (16)	Our results highlight the risk in assuming a perioperative beta-blocker regimen has benefit without substantial harm, and the importance and need for large randomised trials in the perioperative setting. Patients are unlikely to accept the risks associated with perioperative extended-release metoprolol.	**"Reversed standard practice, so that beta-blockers are no longer used routinely for prophylaxis against perioperative myocardial infarction"**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
A randomised three-arm multicentre comparison of 1 year and 2 years of Herceptin, versus no Herception in women with HER2-positive primary breast cancer who have completed adjuvant chemotherapy.	ANZBCTG	2005	5,102	Data were available for 1694 women randomly assigned to two years of treatment with trastuzumab, 1694 women assigned to one year of trastuzumab, and 1693 women assigned to observation. We report here the results only of treatment with trastuzumab for one year or observation. At the first planned interim analysis (median follow-up of one year), 347 events (recurrence of breast cancer, contralateral breast cancer, second nonbreast malignant disease, or death) were observed: 127 events in the trastuzumab group and 220 in the observation group. The unadjusted hazard ratio for an event in the trastuzumab group, as compared with the observation group, was 0.54 (95 percent confidence interval, 0.43 to 0.67; P<0.0001 by the log-rank test, crossing the interim analysis boundary), representing an absolute benefit in terms of disease-free survival at two years of 8.4 percentage points. Overall survival in the two groups was not significantly different (29 deaths with trastuzumab vs. 37 with observation). Severe cardiotoxicity developed in 0.5 percent of the women who were treated with trastuzumab. N Engl J Med. 2005 Oct 20;353(16):1659-72 (17)	One year of treatment with trastuzumab after adjuvant chemotherapy significantly improves disease-free survival among women with HER2-positive breast cancer.	**"The publication of the ANZ 0101/BIG 1-01 HERA trial which investigated adjuvant trastuzumab led to the registration and PBS [Pharmaceutical Benefits Scheme] funding of this therapy for Australian women with early breast cancer in October 2006."**
Phase III randomised, multi-centre, international trial to determine the relation between dose and clinical activity of STI—571 in patients with unresectable or metastatic malignant gastrointestinal stromal tumors expressing the c—kit receptor tyrosine kinase (CD117).	AGITG	2004	946	At median follow-up of 760 days (IQR 644-859), 263 (56%) of 473 patients allocated imatinib once a day had progressed compared with 235 (50%) of 473 who were assigned treatment twice a day (estimated hazard ratio 0.82 [95% CI 0.69-0.98]; p=0.026). Side-effects arose in 465/470 (99%) patients allocated the once daily regimen compared with 468/472 (99%) assigned treatment twice a day. By comparison with the group treated once a day, more dose reductions (77 [16%] vs 282 [60%]) and treatment interruptions (189 [40%] vs 302 [64%]) were recorded in patients allocated the twice daily regimen, but treatment in both arms was fairly well tolerated. 52 (5%) patients achieved a complete response, 442 (47%) a partial response, and 300 (32%) stable disease, with no difference between groups. Median time to best response was 107 days (IQR 58-172). Lancet. 2004 Sep 25-Oct 1;364(9440):1127-34 (18)	If response induction is the only aim of treatment, a daily dose of 400 mg of imatinib is sufficient; however, a dose of 400 mg twice a day achieves significantly longer progression-free survival.	**"This trial radically changed standard of care for patients with advanced GIST [Gastrointestinal stromal tumour] and is now entrenched in clinical practice and Glivec is reimbursed internationally for this indication"**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
Clots in Legs or TEDS after Stroke - A randomised trial to establish the effectiveness of graduated compression stockings (GCS) to prevent post stroke deep venous thrombosis and pulmonary embolism (PE).	ASTN	2009	2,518	All patients were included in the analyses. The primary outcome occurred in 126 (10·0%) patients allocated to thigh-length (Graduated Compression Stockings) GCS and in 133 (10·5%) allocated to avoid GCS, resulting in a non-significant absolute reduction in risk of 0·5% (95% CI −1·9% to 2·9%). Skin breaks, ulcers, blisters, and skin necrosis were significantly more common in patients allocated to GCS than in those allocated to avoid their use (64 [5%] vs 16 [1%]; odds ratio 4·18, 95% CI 2·40–7·27). Lancet. 2009 Jun 6; 373 (9679): 1958-65 (19)	These data do not lend support to the use of thigh-length GCS in patients admitted to hospital with acute stroke. National guidelines for stroke might need to be revised on the basis of these results.	**"Incorporated into International guidelines with major shift in international practice".**
Adjuvant radiotherapy versus observation alone for patients at risk of lymph-node field relapse after therapeutic lymphadenectomy for melanoma: a randomised trial.	ANZMTG / TROG	2012	250	123 patients were randomly allocated to the adjuvant radiotherapy group and 127 to the observation group between March 20, 2002, and Sept 21, 2007. Two patients withdrew consent and 31 had a major eligibility infringement as decided by the independent data monitoring committee, resulting in 217 eligible for the primary analysis (109 in the adjuvant radiotherapy group and 108 in the observation group). Median follow-up was 40 months (IQR 27-55). Risk of lymph-node field relapse was significantly reduced in the adjuvant radiotherapy group compared with the observation group (20 relapses in the radiotherapy group vs 34 in the observation group, hazard ratio [HR] 0·56, 95% CI 0·32-0·98; p=0·041), but no differences were noted for relapse-free survival (70 vs 73 events, HR 0·91, 95% CI 0·65-1·26; p=0·56) or overall survival (59 vs 47 deaths, HR 1·37, 95% CI 0·94-2·01; p=0·12). The most common grade 3 and 4 adverse events were seroma (nine in the radiotherapy group vs 11 in the observation group), radiation dermatitis (19 in the radiotherapy group), and wound infection (three in the radiotherapy group vs seven in the observation group). Lancet Oncol. 2012 Jun; 13(6):589-97 (20)	Adjuvant radiotherapy improves lymph-node field control in patients at high risk of lymph-node field relapse after therapeutic lymphadenectomy for metastatic melanoma. Adjuvant radiotherapy should be discussed with patients at high risk of relapse after lymphadenectomy.	**"This trial proved the efficacy of radiotherapy in managing local recurrence for patients with evidence of melanoma in their lymph nodes (stage III disease). This will change treatment guidelines."**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
The safety of addition of nitrous oxide to general anaesthesia in at-risk patients having major non-cardiac surgery (ENIGMA-II): a randomised, single-blind trial.	ANZCA CTN	2014	7,112	Of 10 102 eligible patients, we enrolled 7112 patients between May 30, 2008, and Sept 28, 2013. 3543 were assigned to receive nitrous oxide and 3569 were assigned not to receive nitrous oxide. 3483 patients receiving nitrous oxide and 3509 not receiving nitrous oxide were assessed for the primary outcome. The primary outcome occurred in 283 (8%) patients receiving nitrous oxide and in 296 (8%) patients not receiving nitrous oxide (relative risk 0·96, 95% CI 0·83–1·12; p=0·64). Surgical site infection occurred in 321 (9%) patients assigned to nitrous oxide, and in 311 (9%) patients in the no-nitrous oxide group (p=0·61), and severe nausea and vomiting occurred in 506 patients (15%) assigned to nitrous oxide and 378 patients (11%) not assigned to nitrous oxide (p<0·0001). Lancet. 2014 Oct; 384(9952):1146-1454 (21)	Our findings support the safety profile of nitrous oxide use in major non-cardiac surgery. Nitrous oxide did not increase the risk of death and cardiovascular complications or surgical-site infection, the emetogenic effect of nitrous oxide can be controlled with antiemetic prophylaxis, and a desired effect of reduced volatile agent use was shown.	**“Re-established the safety of nitrous oxide anaesthesia. Incorporated into international guidelines”**
AC [Adriamycin & Doxorubicin] and x 4 followed by CMF [Cyclophosphamide, Methotrexate & Fluorouracil] x 3 with or without a chemotherapy-free interval, +/- tamoxifen versus toremifene for premenopausal and perimenopausal patients with node-positive breast cancer who are not suitable for endocrine therapy alone.	ANZBCTG	2004	1,035	Toremifene and tamoxifen yielded similar disease-free (DFS) and overall survival (OS): 5-year DFS rates of 72% and 69%, respectively [risk ratio (RR)=0.95; 95% confidence interval (CI)=0.76–1.18]; 5-year OS rates of 85% and 81%, respectively (RR = 1.03; 95% CI = 0.78–1.36). Similar outcomes were observed in the ER-positive cohort. Toxicities were similar in the two treatment groups with very few women (<1%) experiencing severe thromboembolic or cerebrovascular complications. Quality of life results were also similar. Nine patients developed early stage endometrial cancer (toremifene, six; tamoxifen, three). Ann Oncol 2004; 15(12):1749-1759 (22)	Toremifene is a valid and safe alternative to tamoxifen in postmenopausal women with endocrine-responsive breast cancer.	**"This study confirmed tamoxifen as standard therapy, and standard chemotherapy without a gap. Incorporated into clinical practice."**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
PeriOperative ISchemic Evaluation-2 Trial (POISE-2).	ANZCA CTN	2014	4,998	The primary outcome (a composite of death or nonfatal myocardial infarction at 30 days) occurred in 351 of 4998 patients (7.0%) in the aspirin group and in 355 of 5012 patients (7.1%) in the placebo group (hazard ratio in the aspirin group, 0.99; 95% confidence interval [CI], 0.86 to 1.15; P=0.92). Major bleeding was more common in the aspirin group than in the placebo group (230 patients [4.6%] vs. 188 patients [3.8%]; hazard ratio, 1.23; 95% CI, 1.01, to 1.49; P=0.04). The primary and secondary outcome results were similar in the two aspirin strata. N Engl J Med. 2014 Apr 17;370(16):1494-503 (23)	Administration of aspirin before surgery and throughout the early postsurgical period had no significant effect on the rate of a composite of death or nonfatal myocardial infarction but increased the risk of major bleeding.	**"Provides definitive guidance to clinicians and has been incorporated into international guidelines"**
A Study pf R1507 in Patients With Recurrent or Refractory Sarcoma.	ASSG	2014	163	From December 2007 through August 2009, 163 eligible patients from 33 institutions were enrolled. The median patient age was 31 years (range, 785 years). Histologic diagnoses included Osteogenic Sarcoma (n = 38), Rhabdomyosarcoma (n = 36), Synovial Sarcoma (n = 23), and other sarcomas (n = 66). The overall objective response rate was 2.5% (95% confidence interval, 0.7%6.2%). Partial responses were observed in 4 patients, including 2 patients with Osteogenic Sarcoma, 1 patient with Rhabdomyosarcoma, and 1 patient with alveolar soft part sarcoma. Four additional patients (3 with Rhabdomyosarcoma and 1 with myxoid liposarcoma) had a ≥ 50% decrease in tumor size that lasted for <4 weeks. The median progression-free survival was 5.7 weeks, and the median overall survival was 11 months. The most common grade 3/4 toxicities were metabolic (12%), hematologic (6%), gastrointestinal (4%), and general constitutional symptoms (8%). Cancer. 2014 Aug 15;120(16):2448-56 (24)	R1507 is safe and well tolerated but has limited activity in patients with recurrent or refractory bone and soft tissue sarcomas. Additional studies to help identify the predictive factors associated with clinical benefit in selected histologies such as Rhabdomyosarcoma appear to be warranted.	**"Substantially advanced understanding of the role of anti-insulin growth factor-1 receptor therapy in sarcoma"**
A Trial of 2 Options for Second Line Combination Antiretroviral Therapy Following Virological Failure of a Standard Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI) + 2N(t)RTI First Line Regimen (SECOND-LINE Trial).	TVRP	2013	541	We enrolled 558 patients, of whom 541 (271 in the control group, 270 in the raltegravir group) were included in the primary analysis. At 48 weeks, 219 (81%) patients in the control group compared with 223 (83%) in the raltegravir group met the primary endpoint (difference 1·8%, 95% CI 4·7 to 8·3), fulfilling the criterion for noninferiority. 993 adverse events occurred in 271 participants in the control group versus 895 in 270 participants in the raltegravir group, the most common being gastrointestinal. Lancet. 2013 Jun 15;381(9883):2091-9 (25)	The raltegravir regimen was no less efficacious than the standard of care and was safe and well tolerated. This simple NtRTI-free treatment strategy might extend the successful public health approach to management of HIV by providing simple, easy to administer, effective, safe, and tolerable second-line combination antiretroviral therapy.	**"Changed both policy and practice, influenced change in treatment guidelines".**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
A Single Arm Phase II Trial of Intraperitoneal Chemotherapy with Paclitaxel and Cisplatin after Optimal Debulking Surgery for Ovarian, Peritonuem and Fallopian Tube Cancers assessing the feasibility, toxicity and effects on quality of life of a modified GOG 172 (Gynaecologic Oncology Group) intraperitoneal (IP) regimen (TRIPOD Trial).	ANZGOG	2013	38	Thirty-eight eligible patients were recruited from 12 sites between July 2007 and December 2009. Seventy-one percent (n=27) completed at least 4 cycles and 63% (n=24) completed all 6 cycles. Grade 3 or 4 adverse events included nausea (n=2), vomiting (n=2), abdominal pain (n=2), and diarrhea (n=1), but not febrile neutropenia, neurotoxicity, or nephropathy. There were no treatment-related deaths. Catheter-related complications were the most frequent cause of early discontinuation of treatment (16 patients, 21%). Apart from neurotoxicity HRQL [health-related quality of life] which worsened over time, Health Related Quality of Life was stable or improved with time. Most patients (≥50%) judged moderate benefits (e.g., an extra 6 months survival time or a 5% improvement in survival rates) necessary to make IP chemotherapy worthwhile. J Gynecol Oncol. 2013 Oct; 24(4): 359–366 (26)	IP chemotherapy was feasible, tolerable, and most participants considered moderate survival benefits sufficient to warrant the adverse effects and inconvenience.	**"Although a phase 2 trial, it demonstrated that it was possible to safely administer intraperitoneal chemotherapy with minor modifications in dose and meticulous attention to preventing and managing adverse effects".**
Randomised comparison of fluid resuscitation with human albumin solution or normal saline among critically ill patients (SAFE, Saline versus Albumin Fluid Evaluation, Study)	ANZICS CTG	2004	6,997	Of the 6997 patients who underwent randomization, 3497 were assigned to receive albumin and 3500 to receive saline; the two groups had similar baseline characteristics. There were 726 deaths in the albumin group, as compared with 729 deaths in the saline group (relative risk of death, 0.99; 95 percent confidence interval, 0.91 to 1.09; P=0.87). The proportion of patients with new single-organ and multiple-organ failure was similar in the two groups (P=0.85). There were no significant differences between the groups in the mean (+/- SD) numbers of days spent in the ICU (6.5+/-6.6 in the albumin group and 6.2+/-6.2 in the saline group, P=0.44), days spent in the hospital (15.3+/-9.6 and 15.6+/-9.6, respectively; P=0.30), days of mechanical ventilation (4.5+/-6.1 and 4.3+/-5.7, respectively; P=0.74), or days of renal-replacement therapy (0.5+/-2.3 and 0.4+/-2.0, respectively; P=0.41). N Engl J Med. 2004 Apr 17;370(16):1494-503 (27)	In patients in the ICU, use of either 4 percent albumin or normal saline for fluid resuscitation results in similar outcomes at 28 days.	**"Impacted both policy and practice, has led to changes in international guidelines. Economic evaluation indicates potential cost savings are in the order of several hundred million dollars per year"**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
Augmented Vs. Normal Renal Replacement Therapy in Severe Acute Renal Failure (ARF).	ANZICS CTG	2009	1,508	Of the 1508 enrolled patients, 747 were randomly assigned to higher-intensity therapy, and 761 to lower-intensity therapy with continuous veno-venous hemo-diafiltration. Data on primary outcomes were available for 1464 patients (97.1%): 721 in the higher-intensity group and 743 in the lower-intensity group. The two study groups had similar baseline characteristics and received the study treatment for an average of 6.3 and 5.9 days, respectively (P=0.35). At 90 days after randomization, 322 deaths had occurred in the higher-intensity group and 332 deaths in the lower-intensity group, for a mortality of 44.7% in each group (odds ratio, 1.00; 95% confidence interval [CI], 0.81 to 1.23; P=0.99). At 90 days, 6.8% of survivors in the higher-intensity group (27 of 399), as compared with 4.4% of survivors in the lower-intensity group (18 of 411), were still receiving renal-replacement therapy (odds ratio, 1.59; 95% CI, 0.86 to 2.92; P=0.14). Hypophosphatemia was more common in the higher-intensity group than in the lower-intensity group (65% vs. 54%, P<0.001). N Eng J Med. 2009 Oct 22;361(17):1627-38 (28)	In critically ill patients with acute kidney injury, treatment with higher-intensity continuous renal-replacement therapy did not reduce mortality at 90 days.	**"Changed practice, reversed trend towards increased filtration rates in continuous Renal Replacement Therapy leading to substantial savings to healthcare systems globally."**
Crystalloid Versus Hydroxyethyl Starch Trial (CHEST)	ANZICS CTG	2012	6,651	A total of 597 of 3315 patients (18.0%) in the Hydroxy-ethyl startch (HES) group and 566 of 3336 (17.0%) in the saline group died (relative risk in the HES group, 1.06; 95% confidence interval [CI], 0.96 to 1.18; P=0.26). There was no significant difference in mortality in six predefined subgroups. Renal-replacement therapy was used in 235 of 3352 patients (7.0%) in the HES group and 196 of 3375 (5.8%) in the saline group (relative risk, 1.21; 95% CI, 1.00 to 1.45; P=0.04). In the HES and saline groups, renal injury occurred in 34.6% and 38.0% of patients, respectively (P=0.005), and renal failure occurred in 10.4% and 9.2% of patients, respectively (P=0.12). HES was associated with significantly more adverse events (5.3% vs. 2.8%, P<0.001). N Eng J Med. 2012 Nov 15;367(20):1901-11 (29)	In patients in the ICU, there was no significant difference in 90day Mortality between patients resuscitated with 6% HES (130/0.4) or saline. However, more patients who received resuscitation with HES were treated with renal-replacement therapy.	**"major changes in both policy and practice, regulators in the UK, Europe and the USA limited or withdrew hydroxyethyl starch products in the critically ill. Substantial global cost savings will accrue from avoidance of a toxic and expensive therapy"**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
A Randomised, double-blind placebo controlled study of subcutaneous ketamine in the management of cancer pain (Ketamine for cancer pain trial).	PaCCSC	2012	185	In all, 185 participants were included in the primary analysis. There was no significant difference between the proportion of positive outcomes (0.04; 95% CI, 0.10 to 0.18; P = .55) in the placebo and intervention arms (response rates, 27% [25 of 92] and 31% [29 of 93]). Pain type (nociceptive v neuropathic) was not a predictor of response. There was almost twice the incidence of adverse events worse than baseline in the ketamine group after day 1 (incidence rate ratio, 1.95; 95% CI, 1.46 to 2.61; P < .001) and throughout the study. Those receiving ketamine were more likely to experience a more severe grade of adverse event per day (odds ratio, 1.09; 95% CI, 1.00 to 1.18; P = .039). The number of patients needed to treat for one additional patient to have a positive outcome from ketamine was 25 (95% CI, six to ∞). The number needed to harm, because of toxicity-related withdrawal, was six (95% CI, four to 13). J Clin Onc. 2012 Oct 10;30(29):3611-7 (30)	Ketamine does not have net clinical benefit when used as an adjunct to opioids and standard coanalgesics in cancer pain.	**"Led to changes in both policy and practice".**
Fetal intrapartum pulse oximetry to reduce operative delivery rates in the presence of a non-reassuring fetal heart rate: a multicentre randomised controlled trial (the FOREMOST trial).	IMPACT	2006	600	There was a statistically significant 23% relative risk reduction in operative delivery for non-reassuring fetal status in the fetal pulse oximetry + cardiotocograph group (n = 75 of 305, 25%), compared with those in the cardiotocograph-only group (n = 95/295, 32%) (relative risk 0.77, 95% confidence interval 0.599, 0.999, P = .048). There were no significant between-group differences in overall operative births (fetal pulse oximetry + cardiotocograph group 73%, cardiotocograph-only group 71%, relative risk 1.04, 95% confidence interval 0.94, 1.15, P = .478) or neonatal outcomes. Am J Obstet Gynecol. 2006 Mar; 194(3):606.e1-16 (31)	The use of fetal pulse oximetry to augment fetal wellbeing assessment during labor resulted in a statistically significant reduction in the operative intervention for non-reassuring fetal status, compared with the use of conventional cardiotocograph monitoring alone. This reduction was achieved with no significant difference in neonatal outcomes.	**"Changed both policy and practice".**
Metformin in gestational diabetes: follow-up of offspring of mothers treated with insulin compared with metformin (MiG:TOFU).	IMPACT	2008	733	Of the 363 women assigned to metformin, 92.6% continued to receive metformin until delivery and 46.3% received supplemental insulin. The rate of the primary composite outcome was 32.0% in the group assigned to metformin and 32.2% in the insulin group (relative risk, 0.99 [corrected]; 95% confidence interval, 0.80 [corrected] to 1.23 [corrected]). More women in the metformin group than in the insulin group stated that they would choose to receive their assigned treatment again (76.6% vs. 27.2%, P<0.001). The rates of other secondary outcomes did not differ significantly between the groups. There were no serious adverse events associated with the use of metformin. New Engl J Med. 2008 May 8;358(19):2003-15 (32)	In women with gestational diabetes mellitus, metformin (alone or with supplemental insulin) is not associated with increased perinatal complications as compared with insulin. The women preferred metformin to insulin treatment.	**"Influenced both policy and practice. Results of the trial offered an oral medication which is as effective as insulin but more acceptable to women and can also be used in remote areas".**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
Bispectral Index (BIS) monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial (B-Aware).	ANZCA CTN	2004	2,463	Of 2463 eligible and consenting patients, 1225 were assigned to the BIS group and 1238 to the routine care group. There were two reports of awareness in the BIS-guided group and 11 reports in the routine care group (p=0·22). BIS-guided anaesthesia reduced the risk of awareness by 82% (95% CI 17–98%). Lancet. 2004 May 29;363(9423):1757-63 (33)	BIS-guided anaesthesia reduces the risk of awareness in at-risk adult surgical patients undergoing relaxant general anaesthesia. With a cost of routine BIS monitoring at US$16 per use in Australia and a number needed to treat of 138, the cost of preventing one case of awareness in high-risk patients is about $2200.	**"This study has influenced practice with bispectral index monitoring being implemented to prevent awareness during anaesthesia".**
Nasal CPAP (continuous positive airway pressure) for very preterm infants at birth: Does it reduce the incidence of chronic lung disease? A randomised controlled trial (COIN148002)	IMPACT	2008	610	At 36 weeks' gestational age, 33.9% of 307 infants who were assigned to receive CPAP had died or had bronchopulmonary dysplasia, as compared with 38.9% of 303 infants who were assigned to receive intubation (odds ratio favouring CPAP, 0.80; 95% confidence interval [CI], 0.58 to 1.12; P=0.19). At 28 days, there was a lower risk of death or need for oxygen therapy in the CPAP group than in the intubation group (odds ratio, 0.63; 95% CI, 0.46 to 0.88; P=0.006). There was little difference in overall mortality. In the CPAP group, 46% of infants were intubated during the first 5 days, and the use of surfactant was halved. The incidence of pneumothorax was 9% in the CPAP group, as compared with 3% in the intubation group (P<0.001). There were no other serious adverse events. The CPAP group had fewer days of ventilation. N Engl J Med. 2008 Feb 14;358(7):700-8 (34)	In infants born at 25 to 28weeks' gestation, early nasal CPAP did not significantly reduce the rate of death or bronchopulmonary dysplasia, as compared with intubation. Even though the CPAP group had more incidences of pneumothorax, fewer infants received oxygen at 28 days, and they had fewer days of ventilation.	**"Both Policy and Practice were impacted by the findings of the study, which indicated that even very small babies could be treated with CPAP from birth leading to reduction of lung injuries rate. Implementation of CPAP has reduced the rate of intubation, ventilation and expenditure on surfactant".**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
Oxaliplatin combined with weekly bolus fluorouracil and leucovorin as surgical adjuvant chemotherapy for stage II and III colon cancer (NSABP C-07).	AGITG	2007	2,407	A total of 2,407 patients (96.6%) of the 2,492 patients randomly assigned were eligible. Median follow-up for patients still alive is 42.5 months. The hazard ratio (FLOX [5-Fluorouracil (5-FU) + Leucovorin (LV) + Oxaliplatin] v FULV [5-FU +LV] is 0.80 (95% CI, 0.69 to 0.93), a 20% risk reduction in favor of FLOX (P < .004). The 3- and 4-year disease-free survival (DFS) rates were 71.8% and 67.0% for FULV and 76.1% and 73.2% for FLOX, respectively. Grade 3 neurosensory toxicity was noted in 8.2% of patients receiving FLOX and in 0.7% of those receiving FULV (P < .001). Hospitalization for diarrhea associated with bowel wall thickening occurred in 5.5% of the patients receiving FLOX and in 3.0% of the patients receiving FULV (P < .01). A total of 1.2% of patients died as a result of any cause within 60 days of receiving chemotherapy, with no significant difference between regimens. J Clin Oncol. 2007 Jun 1;25(16):2198-204 (35)	The addition of oxaliplatin to weekly FULV significantly improved DFS in patients with stage II and III colon cancer. FLOX can be recommended as an effective option in clinical practice.	**"As a result of the trial, the use of these chemotherapy drugs is now standard treatment in Stage 3 colon cancer".**
Australasian Collaborative Trial of repeat doses of corticosteroids for the prevention of neonate respiratory disease: a randomised controlled trial (ACTORDS trial).	IMPACT	2006	982	Fewer babies exposed to repeat corticosteroids had respiratory distress syndrome(33%vs 41%; relative risk 0.82, 95% CI 0.710.95, p=0.01) and fewer had severe lung disease (12%vs 20%; relative risk 0.60, 95% CI 0.460.79, p=0.0003) than those in the placebo group. In keeping with these benefits, babies exposed to repeat corticosteroids needed less oxygen therapy (p=0.03), and shorter duration of mechanical ventilation (p=0.01). Mean weight, length, and head circumference at birth and hospital discharge did not differ between treatment groups. Z-scores for weight (p=0.04) and head circumference (p=0.03) at birth were lower in the babies who received repeat corticosteroids although at the time of hospital discharge Z-scores did not differ between treatment groups (p=0.29 for weight, p=0.48 for head circumference). Lancet. 2006 Jun 10; 367(9526):1913-9 (36)	Exposure to repeat doses of antenatal corticosteroids reduces neonatal morbidity. Pending long-term outcome results, the short-term benefits for the babies in our study support the use of repeat doses of corticosteroids in women who remain at risk of very preterm birth 7 or more days after an initial course.	**"Changed both policy and practice. Repeat antenatal corticosteroids have been recommended in Antenatal Corticosteroid Clinical Practice Guidelines."**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
Erlotinib Plus Gemcitabine Compared with Gemcitabine Alone in Patients with Advanced Pancreatic Cancer: A Phase III Trial of the National Cancer Institute of Canada Clinical Trials Group.	AGITG	2007	569	A total of 569 patients were randomly assigned. Overall survival based on an intent-to-treat analysis was significantly prolonged on the erlotinib/gemcitabine arm with a hazard ratio (HR) of 0.82 (95% CI, 0.69 to 0.99; P = .038, adjusted for stratification factors; median 6.24 months v 5.91 months). One-year survival was also greater with erlotinib plus gemcitabine (23% v 17%; P = .023). Progression-free survival was significantly longer with erlotinib plus gemcitabine with an estimated HR of 0.77 (95% CI, 0.64 to 0.92; P = .004). Objective response rates were not significantly different between the arms, although more patients on erlotinib had disease stabilization. There was a higher incidence of some adverse events with erlotinib plus gemcitabine, but most were grade 1 or 2. J Clin Oncol. 2007 May 20; 25(15): 1960-6 (37)	To our knowledge, this randomized phase III trial is the first to demonstrate statistically significantly improved survival in advanced pancreatic cancer by adding any agent to gemcitabine. The recommended dose of erlotinib with gemcitabine for this indication is 100 mg/d.	**"This pivotal trial led to a change in practice with gemcitabine and tarceva being accepted as a new standard based on the statistically improved overall survival in advanced pancreatic cancer. Tarceva was subsequently registered for patients with advanced pancreatic cancer".**
A Randomised trial of exemestane after two to three years of tamoxifen therapy in postmenopausal women with primary breast cancer.	ANZBCTG	2004	4,742	Of the 4742 patients enrolled, 2362 were randomly assigned to switch to exemestane, and 2380 to continue to receive tamoxifen. After a median follow-up of 30.6 months, 449 first events (local or metastatic recurrence, contralateral breast cancer, or death) were reported — 183 in the exemestane group and 266 in the tamoxifen group. The unadjusted hazard ratio in the exemestane group as compared with the tamoxifen group was 0.68 (95 percent confidence interval, 0.56 to 0.82; P<0.001 by the log-rank test), representing a 32 percent reduction in risk and corresponding to an absolute benefit in terms of disease-free survival of 4.7 percent (95 percent confidence interval, 2.6 to 6.8) at three years after randomization. Overall survival was not significantly different in the two groups, with 93 deaths occurring in the exemestane group and 106 in the tamoxifen group. Severe toxic effects of exemestane were rare. Contralateral breast cancer occurred in 20 patients in the tamoxifen group and 9 in the exemestane group (P=0.04). N Engl J Med. 2004 Mar 11;350(11):1081-92 (38)	Exemestane therapy after two to three years of tamoxifen therapy significantly improved disease-free survival as compared with the standard five years of tamoxifen treatment.	**"Longer term data, reported in 2009 after 91 months of follow up, demonstrated a significant survival benefit for patients who were switched to exemestane compared to those who stayed on tamoxifen. Changed clinical practice."**

Clinical Trial	Network	Pub Year	Sample Size	Published Abstract Findings	Published Abstract Conclusion/Interpretation	Description of Impact on Clinical Practice / Policy
Capecitabine versus classical cyclophosphamide, methotrexate, and fluorouracil as first-line chemotherapy for advanced breast cancer.	ANZBCTG	2011	465	Quality-adjusted PFS (P = .2), objective tumor response rate (20%; P = .8), and PFS (median, 6 months; hazard ratio [HR], 0.86; 95% CI, 0.67 to 1.10; P = .2) were similar in women assigned capecitabine versus CMF [Fluorouracil]. OS was longer in women assigned capecitabine rather than CMF (median, 22 v 18 months; HR, 0.72; 95% CI, 0.55 to 0.94; P = .02). Febrile neutropenia, infection, stomatitis, and serious adverse events were more common with CMF; hand-foot syndrome was more common with capecitabine. J Clin Oncol. 2011 Dec 1;29(34):4498-504 (39)	Capecitabine improved OS by being similarly active, less toxic, and more tolerable than CMF. Capecitabine is a good first-line chemotherapy option for women with advanced breast cancer who are unsuited to more intensive regimens.	**"Women receiving capecitabine had superior overall survival, with a favourable toxicity profile allowing longer duration of treatment. These results increased the confidence with which clinicians from Australia and New Zealand might choose a relatively low impact chemotherapy regimen for their patients, without compromising outcomes."**
A multi-centre, randomised controlled trial of the effects of early goal-directed therapy, compared to standard care, on 90-day mortality in patients presenting to the Emergency Department with severe sepsis in Australasia (ARISE RCT).	ANZICS CTG	2014	1,600	Of the 1600 enrolled patients, 796 were assigned to the EGDT group and 804 to the usual-care group. Primary outcome data were available for more than 99% of the patients. Patients in the EGDT group received a larger mean (±SD) volume of intravenous fluids in the first 6 hours after randomization than did those in the usual-care group (1964±1415 ml vs. 1713±1401 ml) and were more likely to receive vasopressor infusions (66.6% vs. 57.8%), red-cell transfusions (13.6% vs. 7.0%), and dobutamine (15.4% vs. 2.6%) (P<0.001 for all comparisons). At 90 days after randomization, 147 deaths had occurred in the EGDT group and 150 had occurred in the usual-care group, for rates of death of 18.6% and 18.8%, respectively (absolute risk difference with EGDT vs. usual care, -0.3 percentage points; 95% confidence interval, -4.1 to 3.6; P=0.90). There was no significant difference in survival time, in-hospital mortality, duration of organ support, or length of hospital stay. N Engl J Med. 2014 Oct 16; 371 (16):1496-506 (40)	In critically ill patients presenting to the emergency department with early septic shock, EGDT did not reduce all-cause mortality at 90 days.	**"Expensive therapy no better than standard care, will influence international guidelines".**

7.2 International recognition and influence

7.2.1 Publication in influential international general medical journals

An analysis of all studies published by networks in the last 10 years was undertaken to identify completed studies that were published in the most influential international general medical journals. All general/internal medical journals with an impact factor >10.00 (*Thomson Reuters, June 2015*) were included in the analysis. These journals were the New England Journal of Medicine (NEJM), The Lancet, the Journal of the American Medical Association (JAMA), Annals of Internal Medicine, British Medical Journal (BMJ), JAMA Internal Medicine (formerly Archives of Internal Medicine) and PLOS Medicine.

A total of 97 studies published by 18 different networks were identified. There were 40 studies published in the Lancet, 34 in the NEJM, nine in the BMJ, eight in JAMA and six articles were published in PLOS Medicine. There were no studies identified in Annals of Internal Medicine or JAMA Internal Medicine. Among these studies there were five prospective cohort studies (observational studies); the remainder were phase II, III or IV clinical trials.

Of note was that for 31 of the studies published in influential international general medical journals, no corresponding data had been recorded to indicate whether the network study had impacted policy or practice (although it would be reasonable to assume that this would be the case).

7.2.2 Citation analysis

The total number of citations for each publication was recorded using the Scopus database. Table 7-2 provides a summary of the number studies published in each journal, the number of networks contributing these publications and the total number of citations recorded as at June 2015. Collectively, these publications have been cited more than 37,400 times with a median (IQR) of 148 (35.5 – 464) citations per publication.

TABLE 7-2 STUDIES PUBLISHED IN INFLUENTIAL INTERNATIONAL GENERAL MEDICAL JOURNALS (N=97)

Journal	No of Publications	No of Networks	Total Citations	Median [IQR] Citations per Publication
Lancet	40	15	10,128	136.5 [40 - 327.5]
NEJM	34	13	25,465	461 [100 - 1,177]
BMJ	9	5	290	21 [4 - 57]
JAMA	8	5	1,501	156.5 [108 - 274]
PLOS Medicine	6	4	58	5 [1 - 5]
Across all five journals	**97**	**18**	**37,442**	**148 [35.5 - 464]**

7.3 International research collaboration

7.3.1 Studies involving international research collaboration

Participating networks were asked to indicate whether a study had involved collaboration with one or more international research groups, and, if so, to provide the name of the research group. Of the total of 1055 published and current network studies that were identified, data to definitively indicate whether a study did or did not involve international collaboration were available only for approximately one quarter of the studies (259/1055 studies). Therefore, the level of international collaboration is likely to be a significant underestimate due to the amount of missing data for this field.

A total of 199 studies were reported to have involved the collaboration of one or more international research groups distributed among 25 networks. There were 60 studies that were definitively reported to have involved no international collaboration. For the remainder of the studies captured as part of the Profiling Networks Project the data were either missing or unknown.

Figure 7.3 shows that approximately 45% (n=89) of studies involving international collaboration had been completed and published, and the remaining 55% (n=110) were underway currently. As reported in Figure 7-4, the vast majority of international collaborative studies reported were phase II, III or IV clinical trials (n=165, 83%) followed by observational studies (n=21, 11%).

FIGURE 7-3 NUMBER OF ALL NETWORK STUDIES INVOLVING INTERNATIONAL COLLABORATION (N=199)

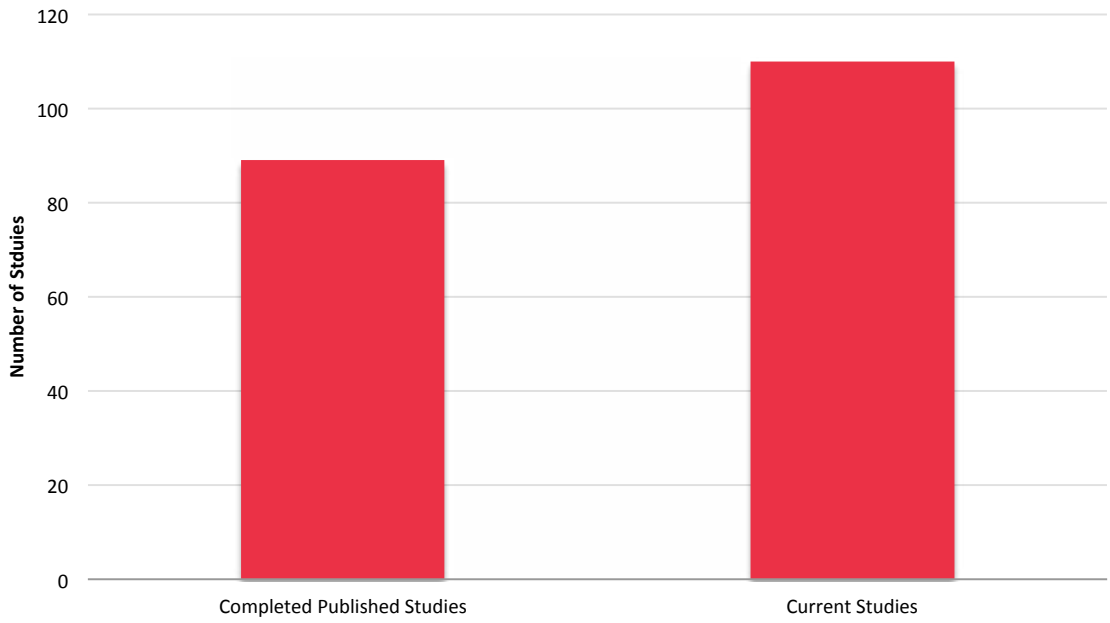
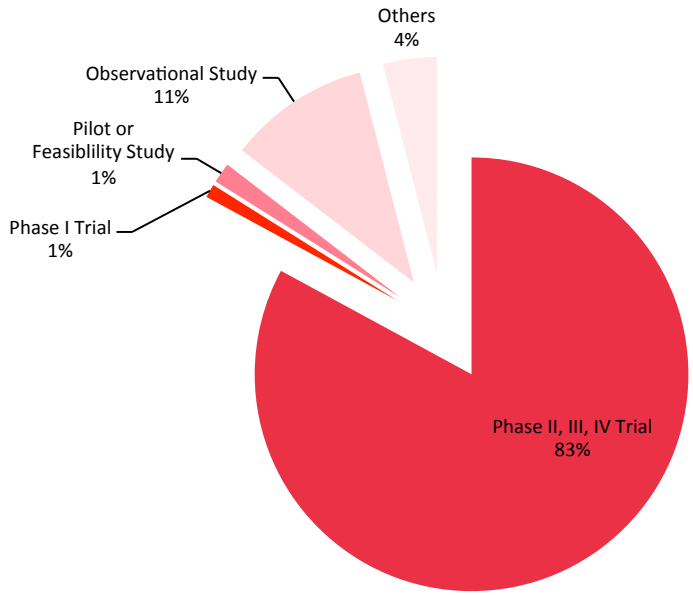
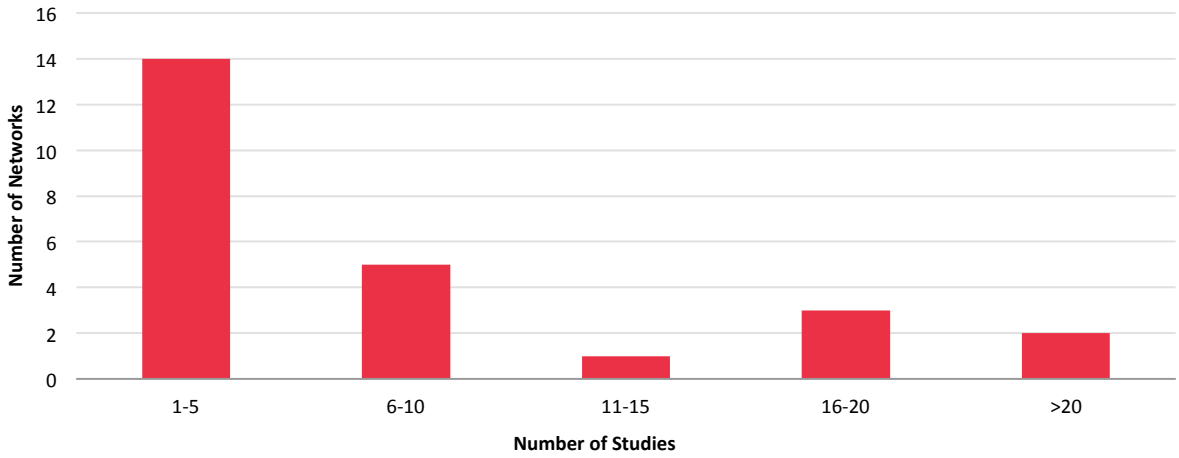


FIGURE 7-4 NUMBER OF ALL NETWORK STUDIES INVOLVING INTERNATIONAL COLLABORATION BY STUDY TYPE (N=199)



The distribution of studies involving international collaboration among participating networks is shown in Figure 7-5. Whilst there were a large number of networks (n=25) that reported at least one international collaborative study, a relatively small number of networks accounted for the majority of studies with five networks reporting more than half (n=111) of the 199 studies with international collaboration.

FIGURE 7-5 NUMBER OF NETWORKS REPORTING STUDIES WITH INTERNATIONAL COLLABORATION (N=25 NETWORKS/199 STUDIES)



As shown in Figure 7-6, just under one third (n=59, 30%) of studies that involved international collaboration were initiated by the network itself, as opposed to instances where networks had collaborated to conduct studies initiated by colleagues overseas (n=119, 60%). This suggests there is a strong degree of global leadership among Australian networks that are designing and leading multinational clinical trials. Among the international collaborative studies that were reported, 15% (n=31) were identified as commercially sponsored studies (see Figure 7-7).

FIGURE 7-6 NUMBER OF ALL NETWORK STUDIES WITH INTERNATIONAL COLLABORATION BY STUDY INITIATOR (N=199)

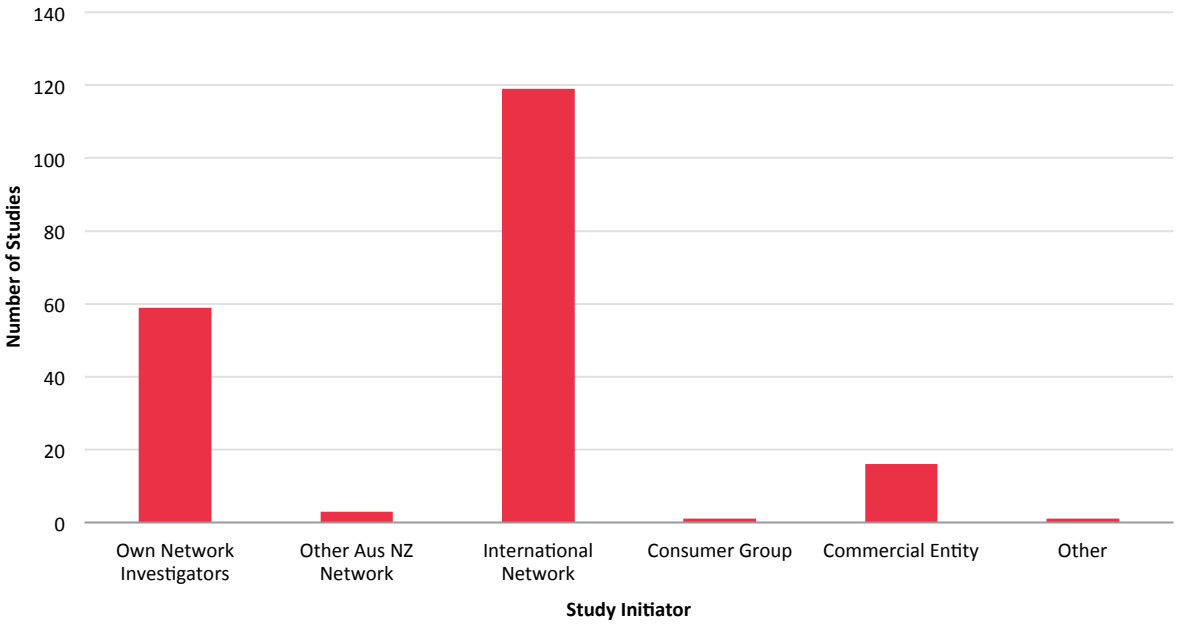


FIGURE 7-7 NUMBER OF STUDIES WITH INTERNATIONAL COLLABORATION BY STUDY SPONSOR (N=197)

7.3.2 Global distribution of research collaboration undertaken by Australian networks

An analysis was undertaken to identify which countries were involved in network studies that were identified as having one or more international collaborators. A substantial number of Australian networks are also active in New Zealand and, therefore no separate analysis of collaborative work that occurs in New Zealand was undertaken. Research groups that were themselves a collaborative of multiple countries were recorded as a 'Multinational Consortium'. Where multiple multinational consortia were reported for a single study these were all recorded (thus a number of studies had several different multinational consortia recorded as an international collaborator). Where multiple national organisations were reported from within a single country, the country was only recorded once as an international collaborator.

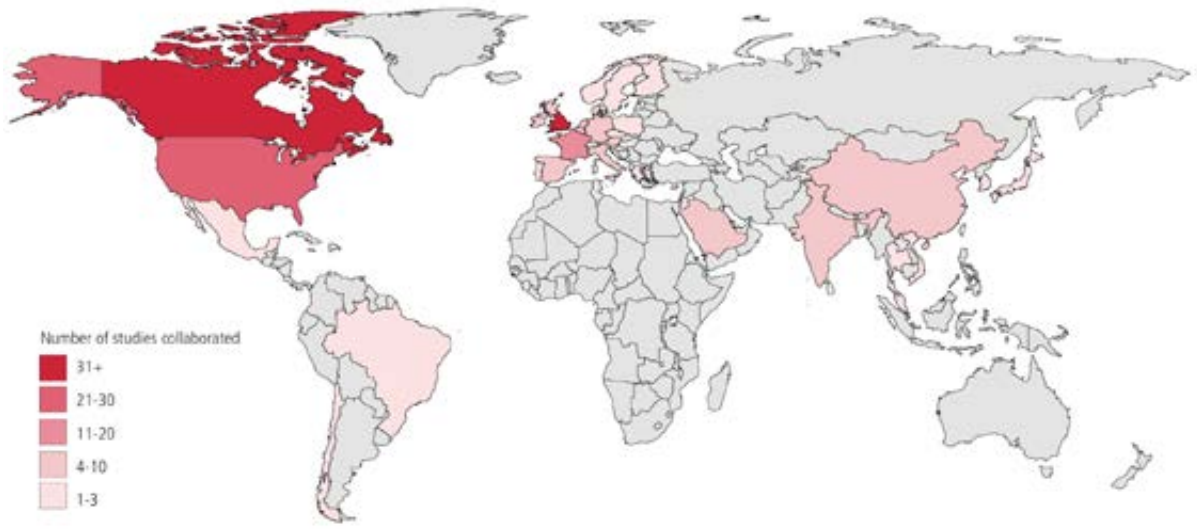
The results of this analysis shown in Table 7-3 and depicted on a global map in Figure 7-8 provide an indication of the high level of international collaboration supported by Australian networks. Of the total of 199 published and current studies that were reported to involve at least one international collaborator, there were 98 different partnerships with multinational consortiums and over 250 individual research collaborations forged with 36 different countries. The most frequently recorded collaborating countries were Canada (n=48), United Kingdom (n=46), United States (n=30) and France (n=18).

TABLE 7-3 NUMBER OF DIFFERENT PARTNERSHIPS WITH INTERNATIONAL RESEARCH GROUPS/CONSORTIA

Collaborator	No of times reported
Multinational Consortium	**98**
1. Canada	46
2. United Kingdom	40
3. United States	30
4. France	18
5. Belgium	9
6. Italy	9
7. Germany	8
8. Scotland	8
9. Singapore	8
10. Spain	7
11. Netherlands	6
12. China	5
13. Denmark	5
14. India	5
15. Ireland	5
16. Saudi Arabia	5
17. Austria	4
18. Brazil	3
19. Chile	3

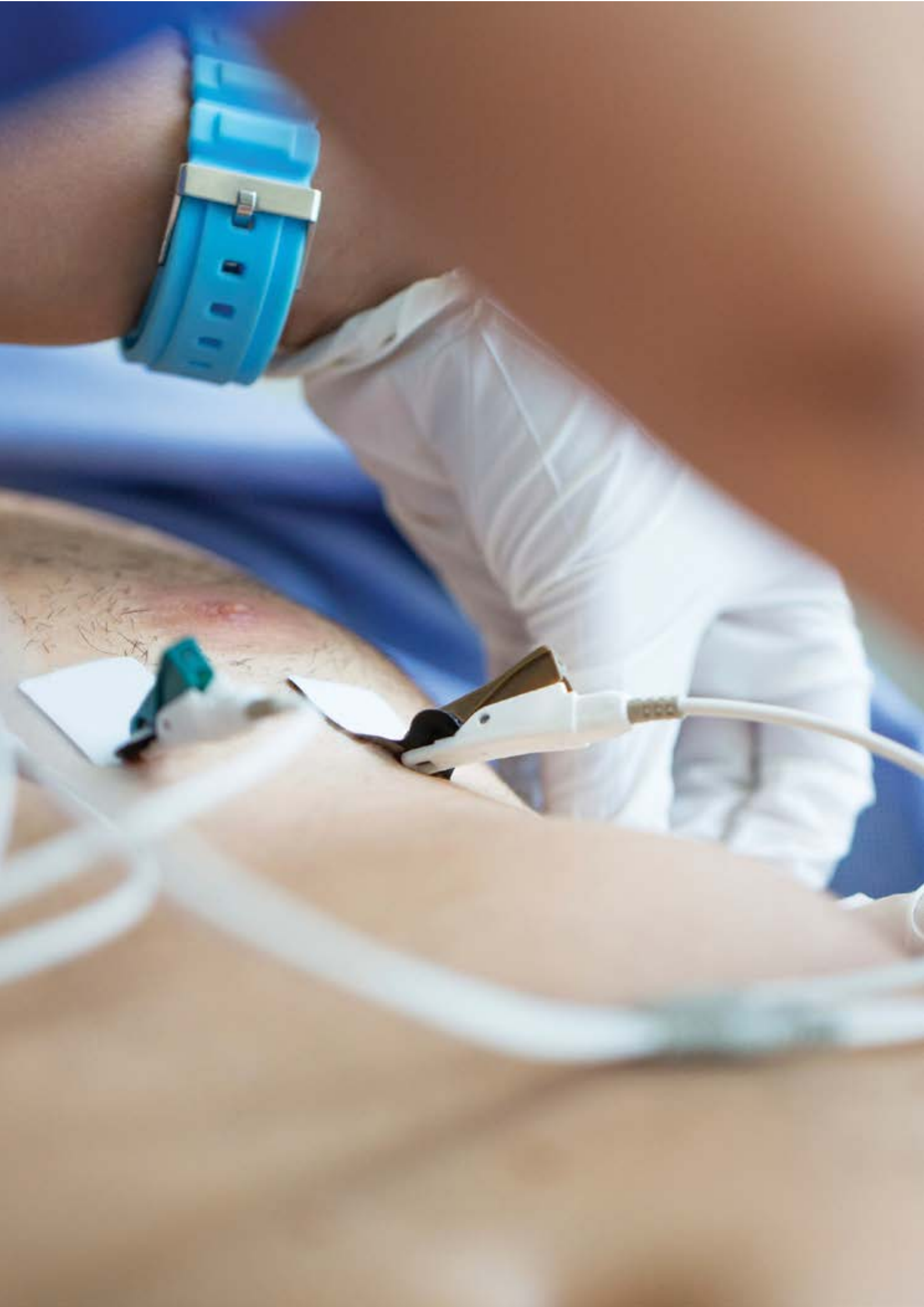
Collaborator	No of times reported
20. Korea	3
21. Poland	3
22. Sweden	3
23. Finland	2
24. Hong Kong	2
25. Japan	2
26. Portugal	2
27. Taiwan	2
28. Greece	1
29. Czech Republic	1
30. Israel	1
31. Northern Ireland	1
32. Malaysia	1
33. Mexico	1
34. Norway	1
35. Thailand	1
36. Vietnam	1
Total	**350**

FIGURE 7-8 GLOBAL MAP OF INTERNATIONAL CLINICAL TRIALS PARTNERSHIPS SUPPORTED BY AUSTRALIAN NETWORKS



7.4 Summary of key findings

- Australian networks reported conducting a large number of studies that provide definitive guidance to clinicians and policymakers to define optimal care. These studies were highly influential with many having been, or likely to be, incorporated into national and international guidelines. Australian networks are making a substantial contribution to the global evidence base in an array of different conditions.
- In the last 10 years, networks have published 97 studies in high impact general medical journals and these manuscripts have generated more than 35,000 Scopus citations. Of note is that the 34 manuscripts published in the NEJM will represent around one third to one half of the nation's publications in this journal during this time period and that the median citation count (461) of these articles indicates a high degree of international influence.
- Data regarding international collaboration was substantially incomplete but even allowing for this limitation there was overwhelming evidence that Australian networks are highly collaborative with international partners and that this includes a large number of international multicentre trials that are led from Australia.



8

Clinical Trials Networks and their Relative Contribution to Clinical Trials Research in Australia

8 Clinical Trials Networks and their Relative Contribution to Clinical Trials Research in Australia

8.1 Overview

This section of the report provides the results of analyses using the linkage of records maintained by the NHMRC for funding awarded for the conduct of clinical trials and clinical trial registration records maintained by the ANZCTR and CT.gov. The aim of these analyses was to develop a better understanding of the relative contribution that networks make to the total clinical trials research activity in Australia and to extract some additional information about network trials that it was not feasible to collect directly from networks as part of this project.

A description of the how data were obtained for both the NHMRC, and ANZCTR/CT.gov analyses, including inclusion and exclusion criteria for linkage, can be found in the methods section of the report. Linkage flowcharts are also provided in Appendix C and D.

8.1.1 NHMRC funding for clinical trials

Data provided by the NHMRC for clinical trial funding was noted to be derived in part from key word searches of information provided by investigators during the grant application process and manual coding of grants as "clinical trial-related" (relevant for grants that were awarded prior to 2010, after which funding for clinical trials was identified as part of the application process using RGMS). In providing these data, the NHMRC makes the qualification that funding data available for the years prior to 2010 may not include some grants that support clinical trials. This was confirmed during the course of undertaking this analysis when a number of grants for clinical trials conducted by networks (n=21) were not included in the clinical trials subset of the main NHMRC funding dataset. A search of 25 randomly selected Project Grants that were identified as clinical trials by NHMRC revealed three grants that were not likely to have been clinical trials based on their title and lay description. Due to NHMRC only capturing certain information after 2010 and inconsistency in the use of 'clinical trials' as a descriptor in research proposals, it was not possible to accurately determine the direct funding that NHMRC has provided to support clinical trials in the last decade.

In addition, funding information could only be obtained for just under half (n=466, 44%) of the studies identified by the participating clinical trials networks. As a consequence, the results reported here are likely to underestimate, possibly substantially, the total number of grants and amount of NHMRC funding that networks have received.

The analysis of NHMRC funding data spanned the years 2000-2014, which is the current timeframe of data reported by the NHMRC for clinical trials-related funding. It was decided to incorporate the years 2000-2004 to maximise the likelihood that NHMRC-funded trials captured within the Profiling Networks Project that were published in 2004 would be included given that it was probable that the trial would have been in receipt of funding within in the four years prior to publication.

8.1.2 Clinical trials registered in Australia

The ANZCTR is an online public registry of clinical trials in Australia, New Zealand and elsewhere that was established in 2005 and is maintained by the NHMRC Clinical Trials Centre, University of Sydney (41). Clinicaltrials.gov (CT.gov) is an online public registry of clinical trials maintained by the United States National Library of Medicine (https://clinicaltrials.gov). Both registries record similar data items but allocated their own unique identifier to each (42).

Data were obtained for all studies coded as "interventional" that were registered on the ANZCTR that were listed as having at least one Australian participating site (n=6,311). As registration on the ANZCTR is not currently mandated within Australia, and there are known to be a number of trials that are either registered solely on CT.gov or duplicated on both registers, staff at the ANZCTR also provided data from the publically available records on CT.gov using the same search parameters (n=4,021).

There were 91 studies that were identified as duplicates appearing in both CT.gov and ANZCTR (where a reciprocal trial register ID number was recorded as a secondary identifier). The datasets were then combined, after removal of redundant duplicate records, and limited only to studies with an anticipated start date of 2004 onwards. This resulted in a total of 9,688 interventional studies that were available for analysis. Trials that had an anticipated start date in 2015 or 2016 were included as the profiling networks project captured as a current study any trial that had received funding so it was possible that some of these trials may have been registered with an anticipated start date of beyond 2014.

Of the 1,055 network studies identified within the Profiling Networks Project, 846 were interventional studies (pilot/feasibility studies or phase I-IV trials). Of these an ANZCTR or CT.Gov ID number was reported by networks or identified by Profiling Networks Project staff for 502 (59%) trials. Among these 502 trials, there were 27 trials that had an ANZCTR ID number recorded that could not be matched in the combined ANZCTR/CT.gov dataset. After additional exclusion for trials with anticipated start dates outside the study period there were 451 trials available for analysis that were included in both the dataset provided by ACTA and one or both of the clinical trial registries. This represents just over half (53%) of the total number of interventional trials that were reported by networks and this needs to be considered when interpreting these results.

The ANZCTR undertakes an annual Data Quality and Completeness Audit and a Trial Duplication Audit. The results of the 2011 Audit reported that 93 of 94 data fields were complete for 148 studies audited (42). It must be noted that whilst there is high completeness of data, there is no requirement currently for trial records to be updated over time. It is therefore reasonable to assume that there may have been trials that recruited sites in Australia after the trial was registered that would not have been captured for this analysis, and trials that were planned but subsequently terminated with minimal or no accrual of participants.

8.2 Examination of clinical trial-related funding data from the NHMRC

8.2.1 NHMRC grants and clinical trial-related funding awarded to clinical trials networks

We identified a total of 974 clinical trial-related grants (excluding Fellowships, Strategic Grants and grants awarded for basic science) for which funding had been distributed in any year between 2000 and 2014 (inclusive). Of these, 200 (21%) were grants awarded to investigators from a clinical trials network that were reported in the Profiling Networks Project. The total funding awarded by the NHMRC for grants that were identified as clinical trial-related for the purpose of this analysis was $988m, of which grants that were identified as having been received by networks accounted for $245m (25%) of the total.

Table 8-1 shows the number of grants and total funding amounts that were awarded from different types of NHMRC grant schemes. Project Grants accounted for the vast majority of funding. There were 871 clinical trial-related Project Grants, totalling $659m, of which 196 (23%) were identified by this project as network grants totalling $212m (32% of total awarded clinical trial-related Project Grant funding).

During the period under consideration, there were 176 NHMRC Project Grants that were awarded a funding amount that was greater than $1m. As shown in Figure 8-1, the proportion of network grants among grants with larger budgets was higher, with 82 (47%) of network grants accounting for half (50%) of all clinical trials-related funding for Project Grants with a budget greater than $1m.

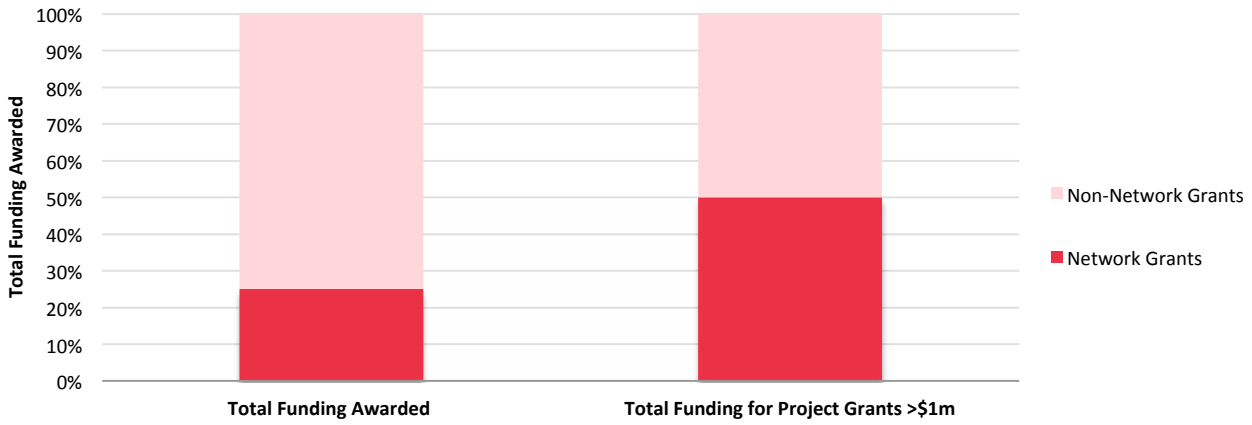
TABLE 8-1: TOTAL FUNDING AWARDED BY NHMRC FOR GRANTS IDENTIFIED AS SUPPORTING CLINICAL TRIALS* THAT RECEIVED FUNDING BETWEEN 2000-2014

Grant Type	Network Grants	Total Clinical Trial-Related Grants*	% of Networks to Total Grants
NHMRC Project Grants	196	871	23%
$ Awarded	$212,350,525	$659,247,137	32%
Program Grants	3	25	12%
$ Awarded	$30,858,209	$228,851,158	13%
Partnership Grants	1	33	3%
$ Awarded	$1,338,280	$28,209,863	5%
Centres for Research Excellence	-	16	-
$ Awarded		$39,344,486	-
Development Grants	-	18	-
$ Awarded		$9,790,135	-
Enabling Grants**	-	11	-
$ Awarded		$22,720,858	-
All Grants	200	974	21%
$ Awarded	$244,547,014	$988,163,637	25%
NHMRC Project Grants over $1m only	**82**	**176**	**47%**
$ Awarded	**$159,518,219**	**$319,890,412**	**50%**

** Excludes Fellowships and Strategic Grants + grants awarded for Basic Science*

*** At least 3 Enabling Grants have been awarded to networks or trial coordinating centres that support network trials but these were not identified within this project as relating to network activities as this project only requested information from networks relating to the funding of projects.*

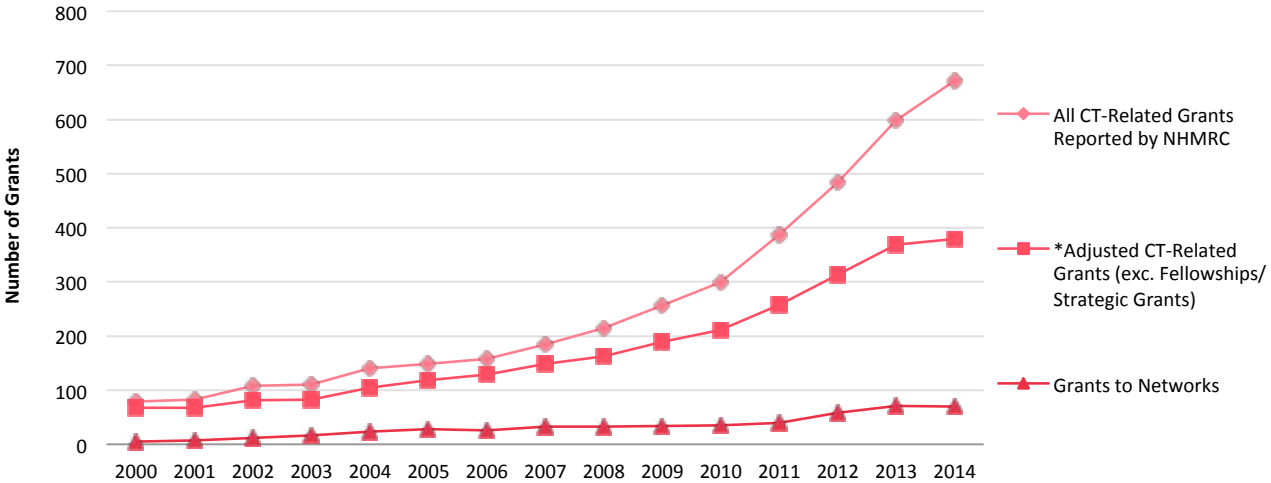
FIGURE 8-1: PROPORTION OF TOTAL FUNDING AWARDED FOR NHMRC CLINICAL TRIAL-RELATED GRANTS THAT RECEIVED FUNDING BETWEEN 2000 AND 2014 (NETWORK/NON-NETWORK)



The number of NHMRC clinical-trial related grants and the associated annual distribution of funds by the NHMRC for each calendar year (2000-2014) are shown in Figure 8-2 and Figure 8-3 respectively. In interpreting these results it should be noted that as most clinical trial grants are multi-year, a single grant will have had funds distributed for several consecutive years.

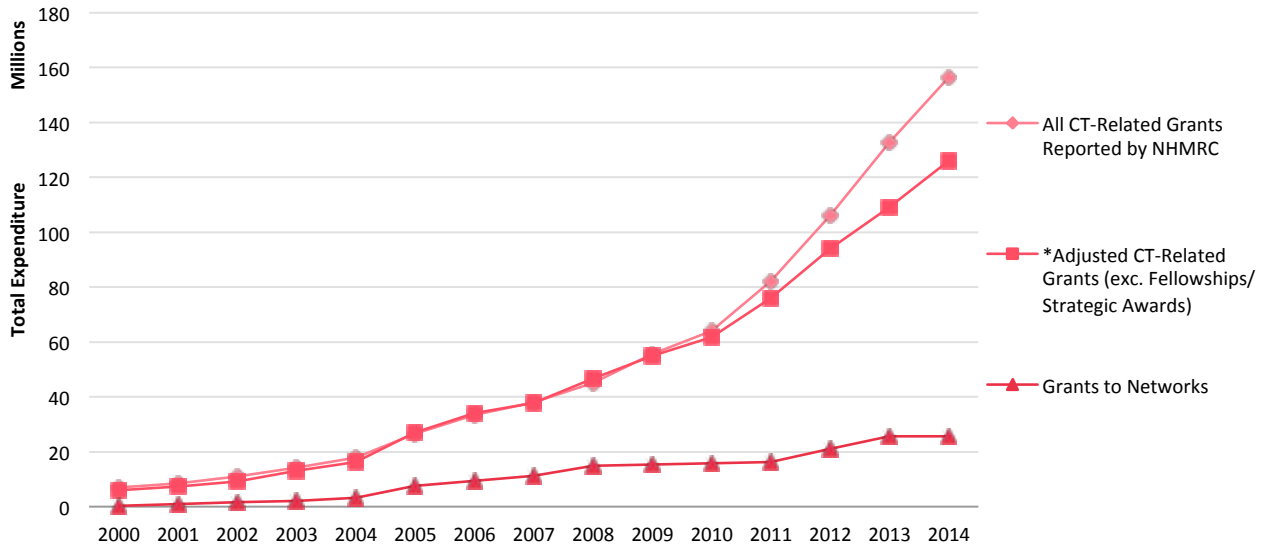
The top series of data has been included to show the total for all grants that are identified and reported by NHMRC as being clinical trial-related, while the middle series of data shows the adjusted total used for this analysis that does not include funding related to Fellowship Grants, Strategic Grants and funding that was identified as supporting projects related to Basic Science. The bottom series shows the total for grants that were awarded to investigators linked to clinical trials networks that were reported to this study.

FIGURE 8-2: NUMBER OF NHMRC CLINICAL TRIAL-RELATED GRANTS THAT RECEIVED FUNDING IN ANY YEAR REPORTED FOR EACH YEAR FROM 2000 TO 2014



** Excludes Fellowships, Strategic Grants and grants awarded for Basic Science*

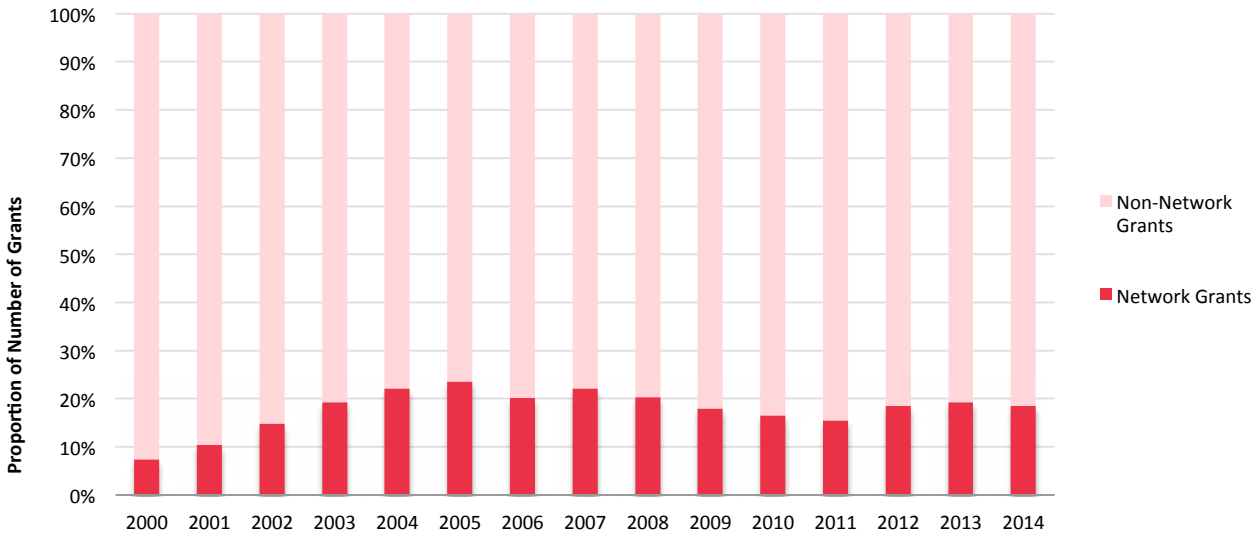
FIGURE 8-3: TOTAL NHMRC EXPENDITURE FOR CLINICAL TRIAL-RELATED GRANTS FOR EACH YEAR FROM 2000 TO 2014



** Excludes Fellowships, Strategic Grants and grants awarded for Basic Science*

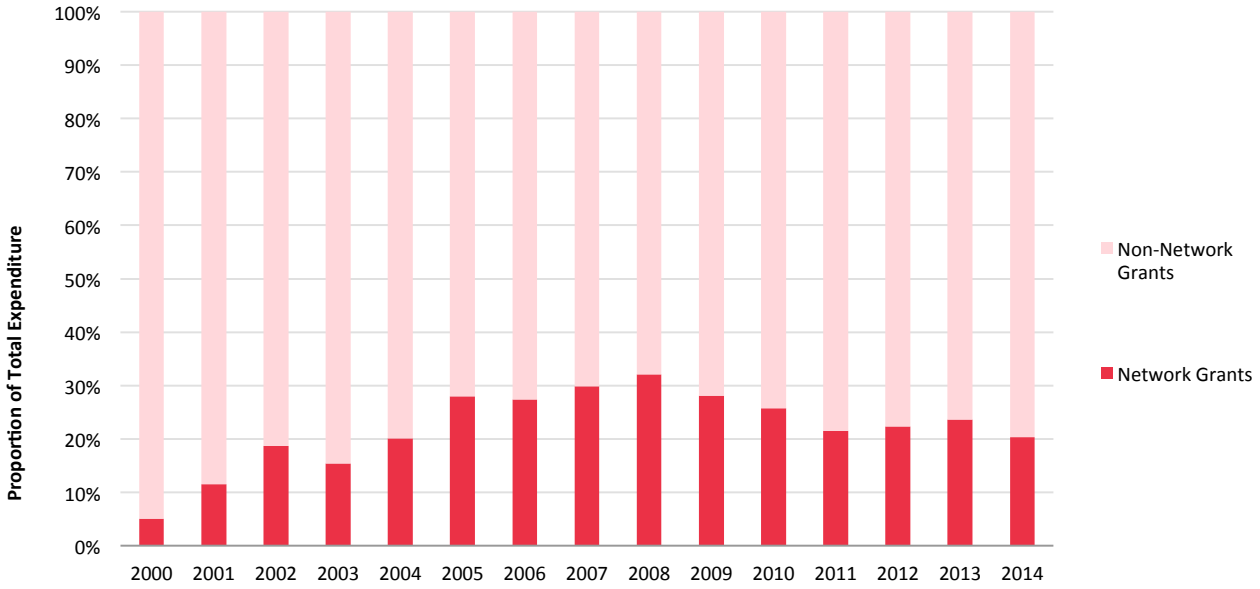
Figure 8-4 and Figure 8-5 show that the proportion of the number of networks trials within the adjusted total number of clinical trial-related grants receiving funding per calendar year has been consistently around 20% over the last 10 years. These grants accounted for a higher relative proportion of the total expenditure in each corresponding year. Between 2005 and 2010, network grants accounted for approximately 25-30% of total expenditure for clinical trial-related funding. This appears to have reduced to 20-25% over the last 4 years (though no test for significance was undertaken).

FIGURE 8-4: PROPORTION OF NUMBER OF NHMRC CLINICAL TRIAL-RELATED GRANTS* RECEIVING DISTRIBUTION OF FUNDING PER YEAR (NETWORK/NON-NETWORK)



** Excludes Fellowships and Strategic Grants + grants awarded for Basic Science*

FIGURE 8-5: PROPORTION OF ANNUAL TOTAL NHMRC EXPENDITURE FOR CLINICAL TRIAL-RELATED GRANTS* PER YEAR (NETWORK/NON-NETWORK)



** Excludes Fellowships and Strategic Grants + grants awarded for Basic Science*

8.2.2 Broad Research Areas and Fields of Research

Figure 8-6 shows the proportion of grants identified by the NHMRC as clinical trial-related grants in each Broad Research Area (excluding Basic Science) that were awarded to clinical trials networks versus non-network grants. Among network grants, 81% (n=163) were in the area of Clinical Medicine and Science, 10% (n=20) were in the area of Public Health and 9% (n=17) were in the area of Health Services Research. Overall, the proportion of grants in the area of Clinical Medicine and Science was higher among network grants than non-network grants.

FIGURE 8-6: BROAD RESEARCH AREA FOR NHMRC CLINICAL-TRIAL RELATED GRANTS 2000-2014 (N=974)

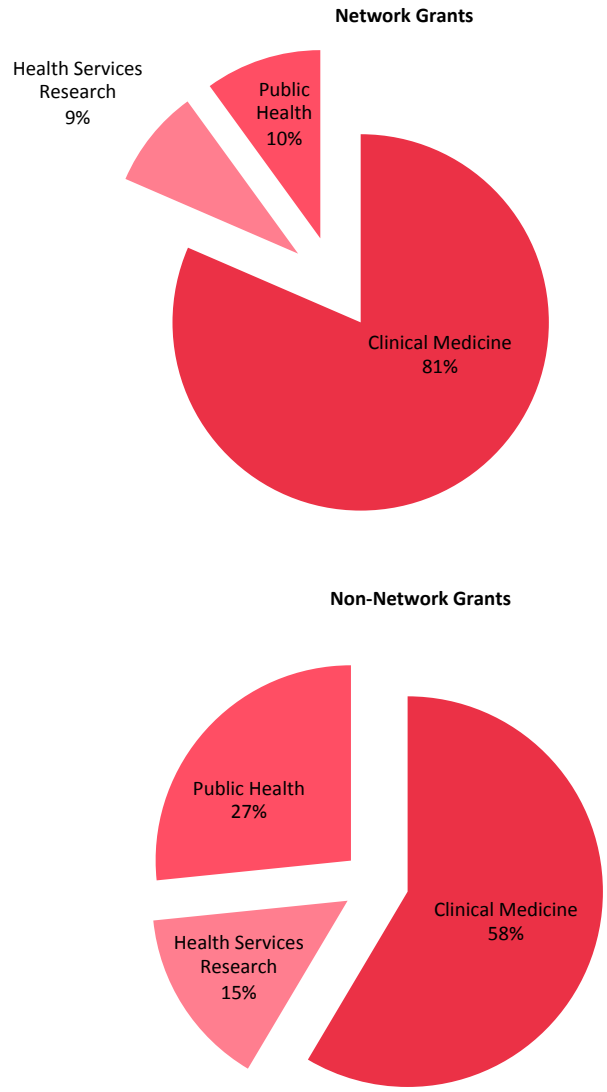


Table 8-2 shows the primary fields of research that were identified for grants awarded to clinical trials networks. Together, grants in the fields of oncology and carcinogenesis (n=27), Paediatrics (n=24), Intensive Care (n=17), Respiratory Diseases (n=9), Anaesthesiology (n=8), Nephrology and Urology (n=8), and Obstetrics and Gynaecology (n=8) accounted for more than 50% of all network grants that were identified.

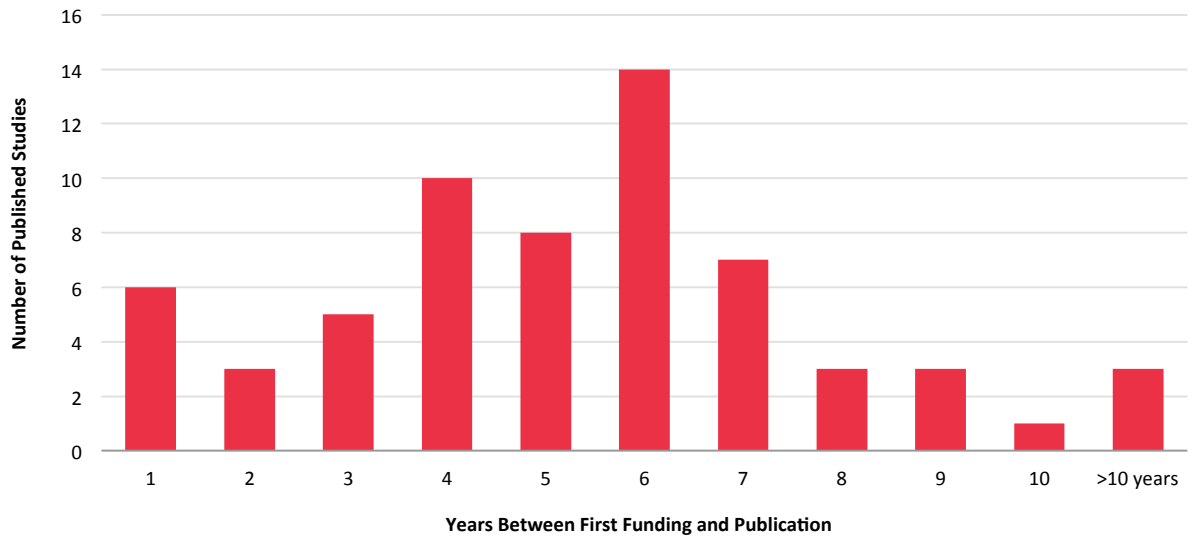
TABLE 8-2: FIELDS OF RESEARCH FOR NHMRC GRANTS TO CLINICAL TRIALS NETWORKS

NHMRC Field of Research Code	Number of Grants
Oncology and Carcinogenesis	27
Paediatrics	24
Intensive Care	17
Respiratory Diseases	9
Anaesthesiology	8
Nephrology and Urology	8
Obstetrics and Gynaecology	8
Clinical Sciences not elsewhere classified	7
Primary Health Care	7
Medical and Health Sciences not elsewhere classified	6
Central Nervous System	5
Infectious Diseases	5
Public Health and Health Services	5
Midwifery	4
Preventive Medicine	4
Surgery	4
Clinical Nursing: Secondary (Acute Care)	3
Health, Clinical and Counselling Psychology	3
Mental Health	3
Neurology and Neuromuscular Diseases	3
Radiation Therapy	3
Radiotherapy and Nuclear Medicine	3
Cancer Therapy (excl. Chemotherapy and Radiation Therapy)	2
Cardiology (incl. Cardiovascular Diseases)	2
Chemotherapy	2
Health Counselling	2
Health Economics	2
Health Promotion	2
Neurosciences	2
Nutrition and Dietetics not elsewhere classified	2
Public Nutrition Intervention	2
Solid Tumours	2
Allergy	1
Clinical and Sports Nutrition	1
Clinical Nursing: Primary (Preventative)	1
Developmental Psychology and Ageing	1
Emergency Medicine	1
Family Care	1
Geriatrics and Gerontology	1
Indigenous Health	1
Nursing not elsewhere classified	1
Orthopaedics	1
Paediatrics and Reproductive Medicine not elsewhere classified	1
Pharmacology and Pharmaceutical Sciences not elsewhere classified	1
Psychology not elsewhere classified	1
Rehabilitation and Therapy (excl. Physiotherapy)	1
Total	**200**

8.2.3 Publication of clinical trial results

Available data were analysed to determine the number of years between a network receiving funding for a clinical trial from the NHMRC, to the year that the primary results of the study were published. Figure 8-7 shows the results for 63 NHMRC-funded clinical trials that were completed and published by networks. The median (IQR) interval from grant funding to publication of the primary results was 5 (4 - 7) years. Just over half of studies (n=32, 51%) were published within 5 years from the year in which they were first funded. Approximately one third (n=21, 34%) were published between 6 and 7 years after their first funding year, and only a relatively small portion (n=7, 11%) were published between 8 and 10 years or more than 10 years (n=3, 5%) later.

FIGURE 8-7: NUMBER OF YEARS FROM FUNDING RECEIVED TO PUBLICATION OF RESULTS FOR NHMRC-FUNDED CLINICAL TRIALS CONDUCTED BY NETWORKS (N=63)



8.3 Analysis of clinical trials registered on the ANZCTR or CT.gov

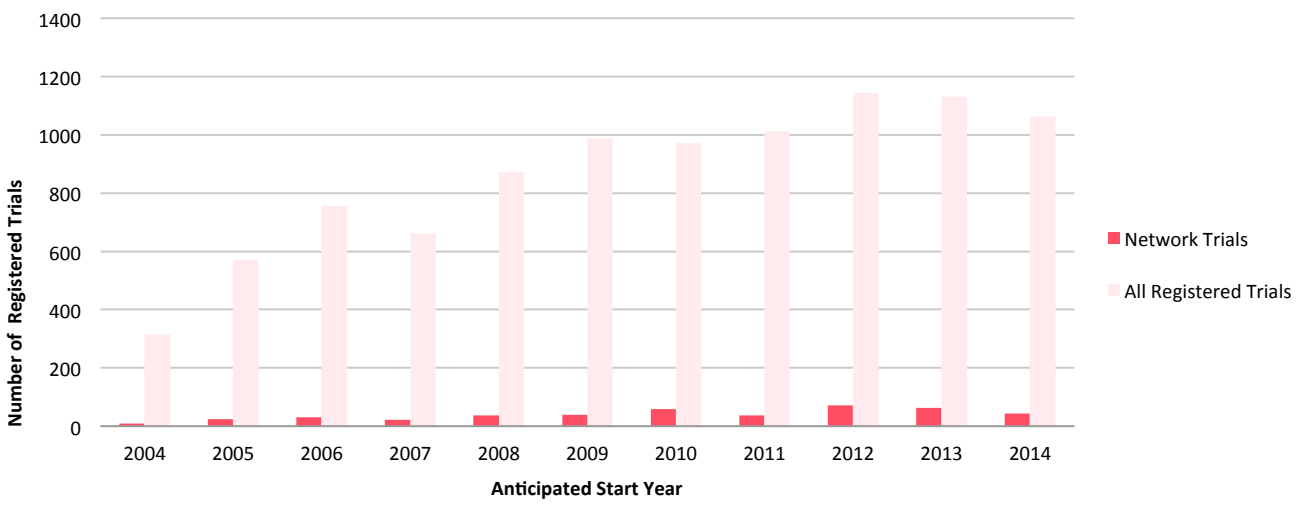
8.3.1 All clinical trials in Australia

Analysis of ANZCTR and CT.gov data indicated that there were a total of 9,688 intervention trials with at least one participating site in Australia that were registered with a planned commencement date of between 2004-2016. There were 846 interventional studies identified by networks as part of the Profiling Network Project, of which 451 were matched on the registers using the search parameters outlined. These 451 trials represented 4.7% of all interventional studies recorded on the trial registers. As shown in Table 8-3 and Figure 8-8, the proportion of network trials to all trials registered in the time period analysed was 4.7%, ranging from 3.2% to 8.7% in any one year.

TABLE 8-3: NETWORK VERSUS NON-NETWORK AUSTRALIAN CLINICAL TRIALS (ALL) REGISTERED ON ANZCTR/CT.GOV BY ANTICIPATED START YEAR

Anticipated Start Year	Matched Network Trials	All Registered Trials	% Network of all Registered Trials
2004	10	314	3.18%
2005	24	570	4.21%
2006	30	757	3.96%
2007	23	662	3.47%
2008	36	872	4.13%
2009	40	986	4.06%
2010	58	972	5.97%
2011	36	1,012	3.56%
2012	71	1,143	6.21%
2013	62	1,131	5.48%
2014	43	1,061	4.05%
2015	13	149	8.72%
2016	0	2	0.00%
No Year Identified	*5*	*56*	*8.93%*
Total All Clinical Trials	**451**	**9,688**	**4.66%**

FIGURE 8-8 NETWORK VERSUS NON-NETWORK AUSTRALIAN CLINICAL TRIALS (ALL) REGISTERED ON ANZCTR/CT.GOV BY ANTICIPATED START YEAR



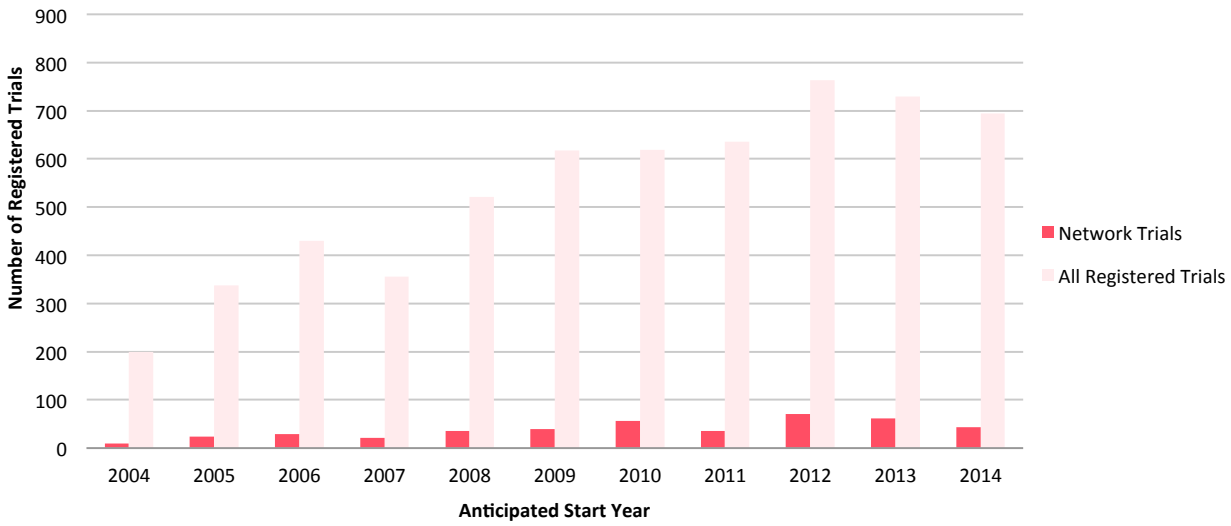
8.3.2 Non-industry sponsored clinical trials in Australia

When industry sponsored trials were excluded, the proportion of network to non-network trials was 7.3% throughout the period that was analysed, with the lowest annual proportion being 5.0% and the highest annual proportion being 12.4% per year (Table 8-4 and Figure 8-9).

TABLE 8-4 NETWORK VERSUS NON-NETWORK AUSTRALIAN CLINICAL TRIALS (NON-INDUSTRY) REGISTERED ON ANZCTR/CT.GOV BY ANTICIPATED START YEAR

Anticipated Start Year	Matched Network Trials (non-industry)	All Registered Trials (non-industry)	% Network of all Registered Trials (non-industry)
2004	10	199	7.35%
2005	24	338	5.03%
2006	29	430	7.10%
2007	21	356	6.74%
2008	35	521	5.90%
2009	40	618	6.72%
2010	57	619	6.47%
2011	36	635	9.21%
2012	71	763	5.67%
2013	61	729	9.31%
2014	43	694	8.37%
2015	13	105	6.20%
2016	0	2	12.38%
No Year Identified	*5*	*47*	*10.63%*
Total Non-Industry Clinical Trials	**445**	**6,056**	**7.35%**

FIGURE 8-9 NETWORK VERSUS NON-NETWORK AUSTRALIAN CLINICAL TRIALS (NON-INDUSTRY) REGISTERED ON ANZCTR/CT.GOV BY ANTICIPATED START YEAR



As shown in Table 8-5, the proportion of non-industry sponsored network trials to non-network trials was highest for phase III trials where 19.0% were identified as network studies. This was followed by phase III/IV trials (15.4% network trials) and phase II trials (13.4% network trials). Only 2.3% of non-industry phase I trials were identified as network trials.

TABLE 8-5 NETWORK VERSUS NON-NETWORK AUSTRALIAN CLINICAL TRIALS (NON-INDUSTRY) REGISTERED ON ANZCTR/CT.GOV BY TRIAL PHASE

Clinical Trial Phase	Matched Network Trials (non-industry)	All Registered Trials (non-industry)	% Network of Registered Trials (non-industry)
Phase 0	1	22	4.55%
Phase I	6	258	2.33%
Phase I/II	5	112	4.46%
Phase II	73	547	13.35%
Phase II/III	9	134	6.72%
Phase III	**98**	**516**	**18.99%**
Phase III/IV	16	104	15.38%
Phase IV	39	612	6.37%
Not applicable or phase not specified	*198*	*3,751*	*5.28%*
Total Non-Industry Clinical Trials	**445**	**6,056**	

When analysed according to planned sample size, approximately one quarter (24.8%, n=77/310) of all non-industry trials that were planning to recruit more than 1,000 participants were network trials (see Table 8-6). However, as reported in sections 5 and 6 of this report, there were an additional 58 trials conducted by networks that were either published or current studies with a sample size of greater than 1,000 participants. As such, the true proportion of all trials with a sample size of more than 1,000 participants undertaken in Australia that are conducted by networks is likely to be substantially higher and could be as much as 50% or more.

TABLE 8-6 NETWORK VERSUS NON-NETWORK AUSTRALIAN CLINICAL TRIALS (NON-INDUSTRY) REGISTERED ON ANZCTR/CT.GOV BY SAMPLE SIZE

Sample Size	Matched Network Trials (non-industry)	All Registered Trials (non-industry)	% Network of Registered Trials (non-industry)
0-50	58	2254	2.57%
51-100	76	1354	5.61%
101-250	115	1286	8.94%
251-500	67	555	12.07%
501-1,000	52	297	17.51%
1,001-2,500	**50**	**185**	**27.03%**
2,501-5,000	**17**	**62**	**27.42%**
>5,000	**10**	**63**	**15.87%**
Total Non-Industry Clinical Trials	**445**	**6056**	

Table 8-7 reports the primary field of research code (MeSH code or equivalent) that was recorded for network trials matched on ANZCTR/CT.gov. The most commonly reported fields were “Cancer” [all cancer-related codes]” (n=148), followed by “Reproductive Health & Childbirth” (n=-75), “Respiratory” (n=36), “Infection” (n=21) and “Diet & Nutrition” (n=20).

TABLE 8-7 PRIMARY FIELDS OF RESEARCH CODES FOR NETWORK TRIALS REGISTERED ON ANZCTR/CT.GOV 2004-2016

Primary Field of Research/MeSH Code for matched network trials registered on ANZCTR/CT.gov	Trials (n)
Cancer (all cancer-related codes)	148
Reproductive Health & Childbirth	75
Respiratory	36
Infection	21
Diet & Nutrition	20
Anaesthesiology	19
Mental Health	17
Public Health	17
Metabolic & Endocrine	10
Stroke	8
Blood	7
Neurological	7
Renal & Urogenital	7
Inflammatory & Immune system	6
Musculoskeletal	3
Alternative and Complementary Medicine	2
Oral & Gastrointestinal	2
Surgery	2
Prostatic Neoplasms	2
Injuries & Accidents	1
Unidentified or Other	*32*
Total Matched Network Trials Registered on ANZCTR/CT.gov	**445**

8.4 Summary of key findings

Proportion of clinical trials funded by the NHMRC

- There were limitations associated with the data that were available from the NHMRC website to determine the proportion of NHMRC funded clinical trials that were conducted by networks. It appears likely that the numerator (network trials funded by the NHMRC) was an underestimate. In addition, it is possible that some grants identified by the NHMRC as supporting clinical trials were either for non-trial activities or only a proportion of the grant was utilised to support trial activities. The lower-end estimate for the proportion of clinical trials that were funded by the NHMRC is around one quarter of trials and one third of funding, although this proportion was around one half for both the number of trials and total funding when the analysis was restricted to large clinical trials with budgets that exceed $1m.
- A further limitation associated with the analysis is that this project collected information from networks about specific funding for projects, but did not capture information about funding from schemes such as the NHMRC Enabling Grant and Centres for Research Excellence schemes that are known to have been received by some networks and will have provided support for network clinical trials in the past 10 years.
- The median interval between the funding of a network trial by the NHMRC and publication of the primary results was 5 years. As such, network clinical trials provide evidence to guide clinical practice and policy within a relatively short period of time.

Proportion of clinical trials registered on the ANZCTR and CT.gov

- Trials conducted by networks represented only a small proportion of all registered trials (5%) and of all non-industry trials (7%), but represented a more substantial proportion of late phase trials (7 to 19%) and an even larger proportion of trials with a sample size of more than 1,000 participants (at least 25%).
- Only just over half of current and published interventional trials conducted by networks could be identified within the trial registries. This was because a trial registration number was not provided by the network and also because subsequent identification of the trial as a network trial proved difficult. It is likely that many of these unidentified trials do have a registration number although it is possible that some trials, particularly those conducted at the beginning of the reporting period for this study, were not captured or that some trials funded recently had not yet been registered. Transcription errors may also have contributed to failure to link between the datasets. A consequence of this is that the number of network trials within registries is likely to have been significantly under-estimated.
- An additional and potentially substantial limitation of this analysis is that while information can be taken to be correct at the time the trial is entered onto the register, and there are fields that are designed to capture updated information n the trial's progress over time, there is no mandatory requirement for records to be updated. As a consequence, it is impossible to accurately determine whether a trial met its recruitment target and was completed.

- Trials may also have several registration numbers that corresponded to sub-studies and it is unclear within the registry where a study with a different registration numbers applies to the same recruited sample of participants.
- The major conclusion is that the capacity to report accurately the proportion of network to non-network trial activity in Australia was severely limited by of the inability to link network trials to details held by clinical trials registries such as ANZCTR and CT.gov, and to how data related to trial progress is captured and reported over time in Australia. Developing solutions to overcome this limitation would enhance substantially an accurate understanding of the size and impact of the sector.

9

Discussion

9 Discussion

9.1 Models of establishing and maintaining networks

9.1.1 Existing networks and their relationship to areas of clinical medicine and public health importance

ACTA identified 37 trials networks in Australia of which 34 networks participated in the study. As such, a strength of this report is that the data presented is based on a significant proportion of all clinical trials conducted by Australian clinical trial networks. However, it is important to note that as the report only utilised data from networks that were active in 2014, it is possible that some networks may have ceased to exist between 2004 and 2014 and that as such, data from and information about these networks would not have not been included within the study.

Only eight of the networks were formed prior to 2000. The formation of new networks appears to be accelerating in recent years, with a wide diversity of disease types and patient categories applicable to an existing network. This acceleration can be interpreted as evidence that communities of clinical researchers view the formation of a network as a useful model for conducting trials and improving the quality of evidence within their discipline.

However, it is notable that there are some areas of major importance to public health for which no network currently exists. In particular, although there are networks that have undertaken trials of surgical procedures and networks that focus on peri-operative medicine, there are no networks that correspond to any surgical speciality. Heart disease, particularly coronary disease, is an area of major importance to public health, and in which major advances have occurred as a consequence of clinical trials, but for which there is no organised clinical trials network in Australia. Mental Health is a National Health Priority Area (NHPA) that is not represented by a national clinical trials network. Some other important physician specialty disciplines, such as respiratory medicine and gastroenterology, also lack a network. Diagnostic medicine also appears to be under-represented.

A key finding is that most networks are self-formed (as opposed to being led externally such as by Government or a consumer-based organisation) and the perceived need for better evidence among clinical leaders is a widespread theme associated with the creation of new networks. The survey only accessed information from established networks and so there is no information to identify the reasons that have contributed to the absence of a network in some disease groups/health states/disciplines. Understanding the barriers and enablers to the formation of new networks may facilitate the creation of network infrastructure across the full range of disciplines that are relevant to the health of our community.

A core paradigm of biomedical research is the chain of translation from basic science discoveries about the fundamental basis of disease mechanisms, the identification of applicable interventions that act on such mechanisms, and the testing of those interventions in clinical trials. Only one network reported that its formation was formed to facilitate the translation of basic science discoveries into clinical trials, and only 4 networks reported having the active involvement of more than 20 basic scientists within their network. It is possible that more interaction between clinical trials networks and basic scientists exists but that this did not emerge because the necessary questions were not asked. However, if the interaction between these groups is relatively limited this may represent a substantial missed opportunity. The design and conduct of

clinical trials is a specialised activity and substantial expertise exists within networks to conduct high quality trials of novel biomedical interventions that have been developed by basic scientists in Australia. Exploring opportunities for greater interaction between networks and the basic science community represents an opportunity to better capitalise on Australia's strengths in both basic and clinical research.

9.1.2 Geographic distribution of network activity

A major strength of the networks is their wide geographical distribution within Australia, as well as the high level of international engagement and collaboration. The networks recruit patients into trials in an enormous number of locations. For example, there are three networks that are active in more than 50 acute hospitals across Australia and networks are also active in sub-acute hospitals and community care facilities.

There are major challenges associated with conducting trials in community-based locations and it is notable that this has not been a barrier to the establishment of several community care-based networks. Moreover, although networks undertake most of their recruitment in metropolitan areas, around 13% of recruitment in Australia is estimated to occur in rural and regional locations although this occurs only for 17 networks that are active in metropolitan as well as rural and regional locations.

A key recommendation of the *Strategic Review of Health and Medical Research Australia* (43) was the embedding of research as part of routine healthcare delivery. Embedding research within vertically integrated academic health science centres that create strong links between basic and clinical scientists at a single geographic location (such as area health service) is one means of embedding research into healthcare. Another model, which has been adopted by clinical trials networks, is the conduct of large and complex multicentre trials across a diverse range of geographic locations that broadly follow the distribution of the Australian population. Such diversity, both in terms of geographic location and the acuity level of the healthcare facility, serves to enhance the generalisability of results obtained from trials. To a very substantial extent what clinical trial networks in Australia are doing on a day-to-day basis, is embedding research into routine healthcare delivery.

Almost all trials conducted by networks enrol patients who would otherwise have received some form of standard care within the healthcare system (as opposed to healthy volunteers). Enrolling those patients into trials where different forms of standard care are compared, or a new intervention is compared against standard care, means that clinicians are constantly asking "how can we deliver health care better?" As such, networks are embedding research in the healthcare system and doing so with a model that is more horizontally than vertically integrated. This integration across geographical and jurisdictional borders serves to maximise access for patients into trials as well as ensure that the results of trials are broadly applicable to the Australian healthcare system.

Many networks have strong international collaboration, through participation in trials that recruit participants overseas, and interaction with international trial coordinating centres. Some international trials involve recruitment in Australia for a trial that has been initiated overseas, while in other situations participants from overseas will be entered into trials that are being led from Australia.

9.1.3 The collaborative nature of networks

A major strength of the networks is their multidisciplinary nature. This embedded 'team-based' approach to clinical trials, embraced by almost all networks, is very likely to result in the conduct of higher quality research because these networks bring together a range of skillsets - each of which is necessary, but not sufficient on their own, for the conduct of high quality trials. While not unique to networks, this drawing

together of a multidisciplinary workforce contributes substantially to the effectiveness and impact of clinical trials.

The depth and breadth of the networks and the extent of their integration with the healthcare system is notable. While the survey is not able to generate precise numbers, many thousands, possibly more than 10,000, clinically active individuals contribute to the conduct of clinical research through clinical trials networks activities in Australia.

In contrast to the depth and strength of their interaction with the healthcare system, the number of networks that have active involvement of consumers is relatively low with only 13 networks reporting active consumer engagement and 9 networks holding regular meetings with consumers. Health consumers have a vital role to play in setting priorities, identifying outcomes that are important to patients, and advocacy. Consumer groups and trial networks have a shared mission and vision to improve healthcare and greater engagement between networks and consumers will likely benefit both groups.

9.1.4 Clinical trials network models: Facilitating and Coordinating Networks

It appears that there are two models of conducting network activity. One model, which we refer to as a 'Facilitating Network', does not conduct or manage trials while the other model, a 'Coordinating Network', undertakes the same range of activities as a Facilitating Network but also directly manages and conducts trials for which it may or may not also be the legal trial sponsor. The Facilitating Network model utilises a collaborating organisation, such as a trial coordinating centre based in a University or MRI, to provide direct trial management and to act as the trial sponsor. This distinction may be partially artificial with some networks, on a project-by-project basis, conducting the trial themselves while out-sourcing trial management for other projects.

It appears that both models work and each network will have its own reasons for why it has adopted one or other model (or a hybrid approach). Nevertheless, in developing policies for the clinical trial network sector it is important that policies are equally applicable to networks using either model. In particular, it is important to note that the cost of coordinating trials exists for both models; it just lies within the network for Coordinating Networks and lies outside of the network for Facilitating Networks. It should be noted that the results presented in Figure 4-6 (Annual Expenditure for Central Network Administration) are likely heavily confounded by each network's model with central network expenditure being much higher for Coordinating Networks with corresponding expenditure for direct trial management not being included with the budgets of Facilitating Networks.

9.1.5 Spectrum of activities undertaken by networks

The participating networks identified a wide range of activities that they undertake to support or conduct trials. This diversity may mean that networks select the spectrum of activities that makes best sense to that network. It is also possible that the range of activities changes with evolution and maturation of a network. However, it is also possible that not all networks have considered the full range of activities and that there may be substantial benefit from interchange and dialogue among the networks.

The vast majority of networks undertake collaborative development of research proposals and provide internal peer review of those proposals as well as run scientific meetings that allow the presentation and discussion of those proposals. This reflects a commitment to a process that will tend to result in the development of higher quality studies that are more likely to be valid, feasible, and capable of high impact. The engagement of networks in activities that enhance the scientific quality of their work on behalf of their

members is one of their major strengths and provides a resource that is somewhat more difficult for non-network-based clinical trial investigators to generate.

It was notable that only seven networks reported involvement in clinical guideline development. This may reflect the view that the networks (and investigators) that generate evidence have an academic conflict of interest and should not contribute to the formation of guidelines that relate to their own research, or that is beyond their brief and/or available resources.

Although 23 networks are engaged in training and education of researchers only 13 had formal mentoring processes for early career researchers. The training of researchers, and particularly early career researchers, is a vitally important activity and perhaps an activity that more networks could contribute to, although almost certainly, much of this mentoring is already occurring at the level of sites and clinical practices.

Further qualitative research about trial network activities and enhancing interchange among networks may identify factors and initiatives that would enhance the effectiveness and efficiency of the sector.

9.1.6 Central network administration and capacity to report research activity

A key finding from the survey was that 28 networks have an Executive Officer or Senior Manager. Among the 26 networks that reported having paid staff, all 26 utilised some or all of their staffing resources for central network administration with 31.39 FTE being allocated to central network administration among these networks. As such, central administration appears to be a core function and among the first, if not the first, activity that is resourced as soon as a network has sufficient funding to pay staff. This provides strong evidence of the vital importance of network administration to the viability of these networks to achieve their mission and vision. It seems reasonable to conclude that a small number of FTE devoted to network administration (31 FTE distributed among 26 networks) play a pivotal and essential role in the viability of the networks that generate the high quality clinical trials activity and outputs for Australia that are reported elsewhere in this report. Anecdotally, obtaining resources for network administration has been a major enabler in the formation and effectiveness of new networks.

It was notable that networks leverage funding from multiple sources and that there are wide ranges of different sources that are used to support central network administration. This is likely to reflect the challenges that networks face in finding the resources to support central network infrastructure. Although this was not addressed directly in the survey, it is widely acknowledged within the sector that obtaining resources for central network administration is a major threat to sustainability and a major barrier for the establishment of new networks.

9.1.7 Role of parent organisations and Cancer Australia

Sixteen networks reported being a sub-entity of an organisation such as a College or professional Society. Research is not generally regarded as 'core business' for Colleges and Societies and so the support provided to so many networks is particularly exemplary. While it is undoubtedly the case that these organisations provide substantial in-kind and indirect support to clinical trials networks, only 3 networks reported receiving direct financial resources from their 'parent' College or Society. Nevertheless, the support and encouragement provided by Colleges and Societies has clearly been critical in establishing and sustaining many of Australia's clinical trials networks.

Cancer Australia also makes a substantial contribution to the effectiveness and sustainability of 12 networks that contributed to this report through the provision of funding based on a triennial cycle to support National co-operative cancer trials groups to develop industry-independent cancer clinical trials protocols. The ultimate aim of this funding is to increase the number of, and participation rates in clinical trials by people affected by cancer in Australia, and to increase the number of clinical sites and clinicians and researchers actively involved in clinical trials (44). Access to funding for central infrastructure for these networks has contributed enormously to the generation of evidence to improve outcomes for patients with cancer in Australia.

9.2 Research activities of clinical trials networks

9.2.1 Completed published studies

Australian networks have contributed very substantially to clinical trials activity in the last 10 years. This report outlines 467 studies completed and published by networks, of which 322 (69%) were phase II/III/IV clinical trials. The networks completed 151 clinical trials with a sample size of more than 250 participants. More than 420,000 participants have been included in network studies published in the last 10 years, of which more than 340,000 have been enrolled in a (interventional) clinical trial. This represents very substantial generation of clinical evidence that can be used by clinicians and policymakers to determine optimal treatment for patients.

The aggregate funding for completed studies is at least $536m. However, this is likely to be a substantial under-estimate of actual total funding. This figure was derived from a sub-set of completed studies that comprised only 34% of studies responsible for 43% of study recruitment. The extent of this under-estimate is difficult to evaluate but could be as much as several hundred million dollars. It should be noted that $200m of total estimated was contributed by two overseas funded trials that included substantial overseas recruitment.

The vast majority of studies conducted by networks are investigator-initiated and will have focussed on questions of relevance to the clinicians who contribute to these networks. Although there were few trials that were initiated by commercial organisations (around 20), there was a larger number of trials with a commercial sponsor (around 40) and even larger number (around 60) with predominant funding from commercial organisations, providing evidence of an increasing level of interaction between networks and commercial organisations.

Whilst data were likely complete for the number of recruited participants, it is not possible to know how much of this recruitment occurred in Australia versus overseas. For multinational studies it is also not possible to know the number of studies, and associated recruitment that occurred in studies that were led from Australia. There were substantial amounts of missing data, particularly related to funding and, to a lesser extent, sponsorship. These all represent limitations that influence the conclusions that can be drawn related to completed studies published by Australian networks.

9.2.2 Current studies

The survey reports a strong ‘pipeline’ of future trial activity that will make a substantial contribution to providing definitive evidence to clinicians and policymakers regarding optimal treatment for patients in Australia. The networks report almost 600 current studies of which more than 400 are phase II/III/IV

clinical trials. The planned sample size for current studies is just over half a million participants of which at least 225,000 have already been recruited. More than 350,000 participants have or will be recruited into phase II/III/IV clinical trials by networks.

In comparison with published clinical trial activity (as reported in section 5) the number of participants being recruited into network studies looks to be substantially higher going forwards. Assuming an average duration of 5 years from study initiation to reporting, average annual current recruitment by networks is likely to be around 100,000 participants per year. This compares favourably with 2013 and 2014 in which the aggregate sample size of trials reported in those years is in the range of 60,000 to 70,000 participants. This is consistent with the increasing number of networks and the likelihood that networks increase their activity progressively over time.

The total funding for current studies is almost half a billion dollars. However, this is likely to be an under-estimate as information on funding was only provided for around half of current studies corresponding to around three quarters of total current recruitment. The NHMRC is the major funder of current studies providing over $200m of support to network studies that are underway currently.

This report is not able to provide accurate information about the number or proportion of network trials that are funded but fail to meet initial or adjusted sample size targets but studies that were terminated early were a very low proportion of all studies. However, this was a prevalence study of currently active studies and may have missed studies funded but terminated previously. Additionally, some of the current studies reported as no longer recruiting but not yet reported, could include some studies that have been funded but have failed to reach their planned sample size.

9.3 Impact of clinical trials networks on the health of Australians and the healthcare system

As reported in detail in Section 7, Australian networks have conducted a large number of studies that provide definitive guidance to clinicians and policymakers, in Australia and internationally, and define optimal care. Whilst an empirical evaluation of the translation and direct impact of these trials on the health system and health outcomes was beyond the scope of this study, many of these studies were reported to have been highly influential and incorporated into national and international guidelines. It is therefore reasonable to conclude that the results of a large number of studies conducted by networks have been implemented into the Australian healthcare system and improved the health outcomes of Australians.

Whilst it is recognised that the translation of the results of clinical trials into practice is often incomplete or lacks the availability of appropriate clinical evidence, clinical trials networks are self-formed and led by Australian clinicians. It is certainly the belief of these networks that the community of clinician-researchers that are created through the formation of networks act as thought-leaders that drive the implementation of trial results of more rapidly and broadly. Further research is needed to provide an accurate estimate of the true value, in terms of benefits to patients, the health system, and broader society, that is created by networks and the high-impact clinical trials that they are able to design and conduct.

9.4 Measurement of clinical trial activity in Australia and the proportion of trials undertaken by networks

9.4.1 Limitations related to information about trial activity and impact provided by networks

It is notable that many networks expressed difficulties associated with finding the resources to complete the survey and having access to the information requested in the survey. This is reflected by the fact that only a small proportion of networks were able to report accurate membership numbers, location of members, location of trial recruitment, numbers of patients recruited, investigators and sites involved in specific trials, grant identification numbers, trial registration numbers, publications, and the practice and policy impact of work conducted by the network.

This could be interpreted as an indication that while many networks have some resources that are used to undertake essential activities, there are many networks with insufficient administration resources to be able to record and report their activities. Among the 32 networks that responded to the corresponding question in the survey, there were 13 who do not maintain any form of database to record network activity. For an area of such importance to the national research effort, it is a critical limitation that so many networks are unable to report their activities in an accurate and timely manner.

9.4.2 Limitations related to clinical trial funding and clinical trial registration data

A key finding of this report was that the completeness and accuracy of data related to trial funding and trial registration substantially limited the capacity of this report to estimate accurately the amount of the clinical trials network activity as a proportion of all clinical trial activity in Australia. Nevertheless, the available data suggests that clinical trials networks are responsible for a sizeable proportion of such activity and that the relative importance of networks is greater for late phase trials with larger sample sizes that represent the predominant source of high quality clinical information that is used by clinicians and policymakers to improve outcomes and health sector productivity.

9.4.3 Measurement of clinical trial activity undertaken by networks

A full exploration of the range of options for measuring and reporting real-time investigator-initiated clinical trial activity was considered to be beyond the scope of this report. However, one novel option to be considered is integrating trial tracking activity with the ethics / governance approval processes in combination with the ANZCTR. Such a system would require mandatory trial registration (currently the National Statement only encourages trial registration) in combination with a unique identifier for each trial site that recruits patients and a unique trial registration number (as exists currently via the ANZCTR). Such a system would need to be able to be integrated to allow linkage with one or more administrative systems and systems that are in use by sites that conduct research to track ethical or governance approvals or both.

A field within the NHMRC's Research Grants Management System that allows the recoding of established networks that are contributing to the study might also facilitate the tracking of funding related to clinical trial network activity. Additionally, being able to distinguish between grant applications that include some planned clinical trial activity from applications that are predominantly or solely a clinical trial may be of assistance. The ANZCTR could also consider collection of grant identifier numbers as a means of linking funding to trial activity.

Finally, many networks appear to have limited access to information systems for recording comprehensive details about their research and outputs and other activities. The development of a dedicated administrative platform for clinical trial networks could substantially increase the amount of data that networks are able to report and would facilitate benchmarking of their activities over time to evaluate the impact of any future efforts that aim to increase the number and quality of investigator-initiated clinical trials in Australia.

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Appendix A: Acknowledgements

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Appendix B: Tables and Figures

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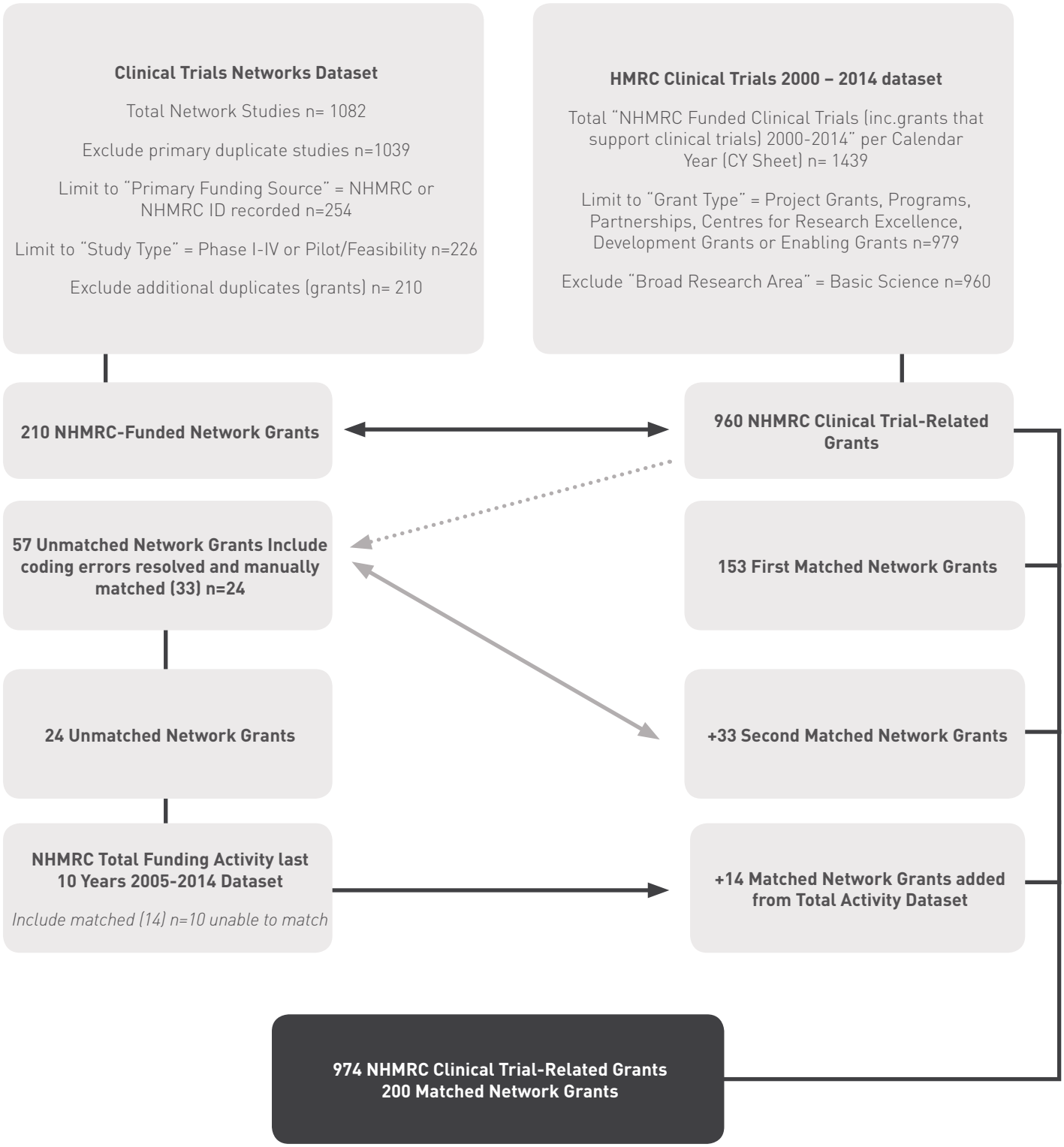
Acronyms

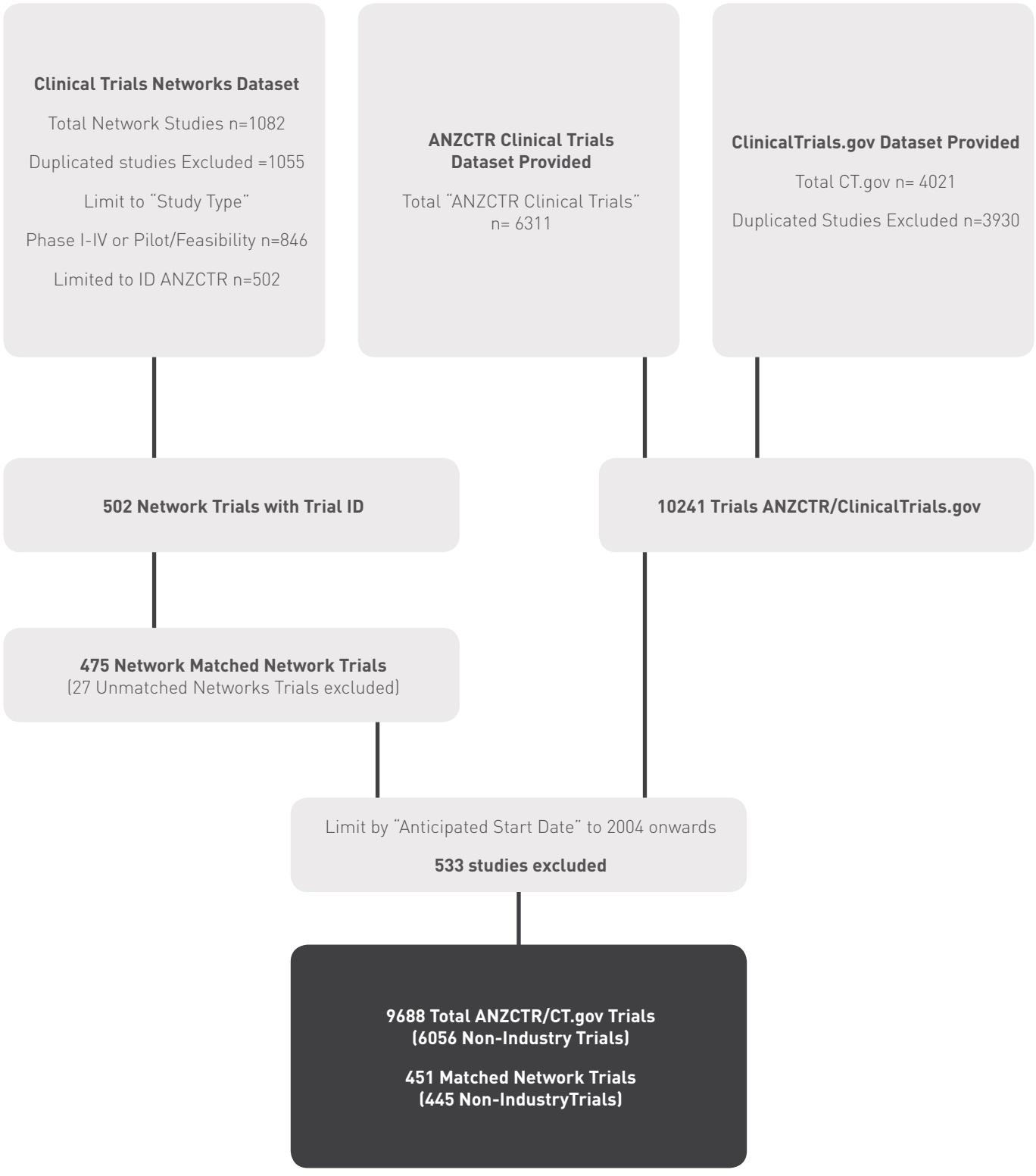
AC4R	The Australasian Consortium of Centres for Clinical Cognitive Research
ACEM CTG	Australia College of Emergency Medicine Trials Group
ACTA	Australian Clinical Trials Alliance
AECTN	Australian Epilepsy Clinical Trials Network
AGITG	Australasian Gastro-Intestinal Trials Group
AKTN	The Australasian Kidney Trials Network
ALTG	Australasian Lung Cancer Trials Group
ANZBCTG	Australian and New Zealand Breast Cancer Trials Group
ANZCA CTN	Australian & New Zealand Intensive Care Society Clinical Trials Group
ANZCTR	Australian New Zealand Clinical Trials Registry
ANZGOG	Australia & New Zealand Gynaecological Oncology Group
ANZICS CTN	Australian and New Zealand Intensive Care Society Clinical Trials Group
ANZMTG	Australia and New Zealand Melanoma Trials Group
ANZMUSC	Australia and New Zealand Musculoskeletal Clinical Trials Group
ANZUP	Australian and New Zealand Urogenital and Prostate Cancer Trials Group
APCReN	Australian Primary Care Research Network
APRN	Australian Paediatric Research Network
ARTnet	Australasian Radiopharmaceutical Trials Network
ASCIN	The Australian Spinal Cord Injury Network
ASSG	Australasian Sarcoma Study Group
ASTN	Australian Stroke Trials Network
ASTN	The Australasian Sleep Trials Network
BMJ	British Medical Journal
BT4K	NSW Better Treatments 4 Kids
COGNO	Cooperative Trials Group for Neuro-Oncology
CT.gov	ClinicalTrials.gov
CTG	Clinical Trials Group
CTN	Clinical Trials Network

EMEA	European Medicines Agency
FDA	Food and Drug Administration (USA)
FTE	Full Time Equivalent
GCIG	Gynecological Cancer InterGroup
ICU	Intensive Care Unit
IMPACT	The Interdisciplinary Maternal Perinatal Australasian Collaborative Trials Network
IQR	Interquartile Range
JAMA	Journal of the American Medical Association
LC	Long Course
MeSH	Medical Subject Headings
MRI	Medical Research Institute
MSRACT	Muscular Sclerosis Research Australia Clinical Trials Network
NEJM	New England Journal of Medicine
NHMRC	National Health and Medical Research Council
NHMRC CTC	NHMRC Clinical Trials Centre, University of Sydney
NHPA	National Health Priority Area
PaCCSC	Palliative Care Clinical Studies Collaborative
PC4	Primary Care Collaborative Cancer Clinical Trial Group
PLOS	Public Library of Science
PoCoG	Psycho-Oncology Co-operative Research Group
PREDICT	Paediatric Research in Emergency Departments International Collaborative
PTNA	Paediatric Trials Network Australia
SC	Short Course
T1DCRN	The Australian Type 1 Diabetes Clinical Research Network
TROG	Trans Tasman Radiation Oncology Group
TVRP	Therapeutic and Vaccine Research Program

Appendix C: NHMRC Data Analysis Process Map



Appendix D: ANZCTR/ClinicalTrials.gov Data Analysis Process Map



Appendix E
Network Profiles

Australasian College for Emergency Medicine Clinical Trials Group

www.acem.org.au

Years	Members	Studies	Funding	Publications
6	NSW, VIC, QLD, WA	2 completed 1 current	$1-250k	2

The Australasian College for Emergency Medicine (ACEM) is a non-for-profit organisation responsible for training emergency physicians and advancement of the professional standards in emergency medicine care across a range of specialised areas in Australia and New Zealand. The Emergency Medicine Clinical Trials Group (ACEM CTG) was established as a subcommittee of the ACEM Scientific Committee with an interest in research and clinical trials in the emergency department setting. It endorses clinical trials related to various aspects of emergency medicine including but not limited to pre-hospital care, emergency department clinical care, disaster response, toxicology, medical education and training, triage and patient flow. While it is a relatively new network, the ACEM CTG has become a peak organisation for emergency medicine in Australasia focused on clinical trials and research in emergency department settings delivering education, advocacy and member support. ACEM CTG promotes and ensures delivery of the best quality emergency medical care research to the community through its committed, expert, flexible and patient-focused approach.

Major Achievements

ACEM CTG has recently published an article which offered a systematic, evidence-based and patient outcome-focussed approach to identify emergency medicine clinical research priorities. The ACEM researcher database was updated in May 2012 and a survey was distributed to emergency physicians (EPs) on this database to ascertain their perceived clinical research priorities. The results of the survey were analysed, and grouped under perceived research priority themes and also as specific research questions.

A consensus meeting 'Finalising research priorities in emergency medicine' hosted in November 2013 introduced and, considering feedback from other members of the CTG, refined a weighting matrix for the ranking of potential research priorities for the ACEM CTG. This framework is expected to determine relevant research questions and projects considered to be of high importance and amenable to multicentre trials.

The network is currently working on an important manuscript, summarising findings of the recently completed large multi-site interventional phase trial TARGET, which recruited 1200 patients across Australia and was conducted to determine the best pain management practice in emergency department settings.

Australasian Gastro-Intestinal Trials Group

www.agitg.org.au

Years	Members	Studies	Funding	Publications
24	Australia wide New Zealand International	26 completed 18 current	>$50m	89

The Australasian Gastro-Intestinal Trials Group (AGITG), formed in 1991, is an independent not-for-profit academic collaborative research group that develops and conducts clinical trials to test new treatments for gastro-intestinal (GI) cancer. The AGITG focuses on identifying gaps in medical knowledge and developing clinical trials that are potentially practice changing in areas of high clinical need. The AGITG continually strives to achieve better health outcomes through GI-related clinical and biological research in Australasia and internationally.

The AGITG is strongly focused on encouraging members of the medical and scientific community to participate in AGITG sponsored clinical trials, with the publication of results and promotion of research outcomes leading to improvements of clinical practice. The membership is actively engaged in the identification and development of novel clinical trial questions and the conduct of a suite of trials addressing both common and rarer GI cancers. Trials are funded by National and State-based granting bodies and local and international pharmaceutical companies.

Major Achievements

An AGITG meta-analysis setting the standard of care for treating people with oesophageal cancer, published in Lancet Oncology, showed for the first time that there is a better chance of survival if patients have chemotherapy and radiation therapy given together just before surgery, rather than surgery alone. The study analysed data from many clinical trials including the AGITG IG9401 trial. It showed conclusively that there is a 14% improvement in survival if patients receive concurrent chemotherapy and radiation therapy before surgery. In March 2008, Lancet Oncology announced that this review was the fourth most read article for 2007.

The international AGITG MAX was a phase III randomised trial of capecitabine, bevacizumab, and mitomycin C in first-line treatment of metastatic colorectal cancer. It demonstrated that adding bevacizumab to capecitabine, with or without mitomycin, significantly improved progression free survival. The study team concluded that with similar overall quality of life and limited adverse events that the combination of capecitabine and bevacizumab should be considered as a first-line therapy option for patients with mCRC, especially those who are unfit for, or who do not require, initial irinotecan or oxaliplatin.

The NCIC/AGITG C0.17 trial, published in the New England Journal of Medicine with AGITG lead investigator Chris Karapetis as first author, detailed response to treatment based on tumour mutation status. CO.17 provided key data in the explanation of the effect of the K-ras status on targeted therapy and has influenced practice worldwide. The AGITG recruited more than half of the patients in this study, demonstrating the influence an AGITG clinical trial has had in routine clinical practice for management of GI tumours worldwide.

Australasian Lung Cancer Trials Group

www.altg.org.au

Years	Members	Studies	Funding	Publications
11	Australia Wide New Zealand	2 completed 1 current	$2.5-10m	3

Founded in 2004, the Australasian Lung Cancer Trials Group (ALTG) is a multi-disciplinary organisation whose mission is to reduce the incidence, morbidity and mortality of lung and other thoracic cancers and improve the quality of life of patients, carers and families in Australia and New Zealand through the coordination and facilitation of high quality clinical research. Membership is available to all medical and non-medical people interested in clinical research in lung and thoracic cancer. The group conducts trials through both international collaborations and cooperative work with the NHMRC Clinical Trials Centre and Peter MacCallum Cancer Centre in Australia.

The ALTG has received Infrastructure Support for Clinical Trials Program under the Strengthening Cancer Care Initiative. The ALTG has been actively involved in developing high-quality trial concepts and supports the active engagement of its 421 clinician, researcher, allied health and consumer members in the initiation, conduct, evaluation and promotion of clinical trials. The group aims to ensure timely publication of its research outcomes in order to contribute to the translation of clinical trials findings into clinical practice and improve the health of lung and thoracic cancer sufferers in Australia and worldwide.

Major Achievements

The MATES study was a randomised phase III trial evaluating the use of thalidomide for maintenance therapy in patients with malignant pleural mesothelioma after first line chemotherapy. Published in Lancet Oncology (2013), this study was a collaborative effort between the ALTG, NHMRC CTC and the Dutch Association of Physicians for Pulmonary Diseases (NVALT).

The B2P2M2 trial was published in Lung Cancer in 2013. This single arm phase II trial evaluated the response rate of BNC105P as second line chemotherapy for patients with advanced malignant pleural mesothelioma.

BR.29 is a double blind randomised trial of cediranib versus placebo in patients receiving paclitaxel/carboplatin chemotherapy for the treatment of advanced or metastatic non-small cell lung cancer and was, published in The European Journal of Cancer in 2014. BR.29 was the result of an international collaboration with the National Cancer Institute of Canada Clinical Trials Group

Australasian Radiopharmaceutical Trials Network

www.agitg.org.au

Years	Members	Studies	Funding	Publications
1	Australia wide New Zealand International	N/A	$10,000-25,000	N/A

The Australasian Radiopharmaceutical Trials network (ARTnet) was officially launched at the 44th Australian and New Zealand Society of Nuclear Medicine (ANZSNM) Annual Scientific Meeting in Adelaide in April 2014 as a joint venture between the ANZSNM and the Australasian Association of Nuclear Medicine Specialists (AANMS). It is a new collaborative network bringing together medical specialists, technologists, scientists and researchers from the field of Nuclear Medicine and Molecular Imaging with a shared interest in multicentre clinical trials utilising radiopharmaceuticals for imaging or therapy.

The network was established to promote and facilitate innovative collaborative clinical research utilising radiopharmaceuticals for imaging and therapy and to develop a network of radiopharmaceutical imaging and therapy sites in Australasia with validated capabilities. It aims to harmonise imaging protocols for research; provide assistance with data collection, analysis and management; and facilitate linkages with other clinical trials networks, the pharmaceutical industry and funding agencies for multicentre clinical trials. ARTnet is striving to support multicentre clinical trials and outcome-based research, and promote collaboration in clinical trials utilising radiopharmaceuticals.

Major Achievements

The establishment of this unique research network has addressed a clearly identified need for a formal research body to support collaborative, multicentre clinical trials utilising radiopharmaceuticals for imaging or therapy. One of the important achievements of this new network was the recent launch of the ARTnet website (www.artnet.org.au) expected to promote public and consumer awareness of radiopharmaceuticals in therapy and imaging and serve as an interface between external organisations (such as pharmaceutical companies), clinical trial groups using functional imaging as an endpoint (e.g. oncology trials using FDG PET/CT) and investigator-initiated trials from within members of the Network.

Whilst ARTnet is a new organisation, it has been approached to provide technical validation for PET-CT imaging at sites participating in the a trial led by the Trans Tasman Radiation Oncology Group, which aims to determine whether breast Magnetic Resonance Imaging and PET-CT are better ways of seeing how breast cancer responds to chemotherapy or hormone therapy compared to mammogram, ultrasound and examination by doctors.

ARTnet, in collaboration with other relevant clinical trials groups, is currently designing a prospective multicentre trial of the impact of Ga-68 PSMA PET imaging in the management of prostate cancer. Ga68 PSMA PET has recently emerged as a very promising imaging agent, with improved accuracy in the detection of prostate cancer. Furthermore, ARTnet has been approached regarding a promising therapeutic initiative, which uses a treatment called radio-immunotherapy to target radiation to tumours in patients with lymphoma.

Australasian Sarcoma Study Group

www.australiansarcomagroup.org

Years	Members	Studies	Funding	Publications
7	Australia Wide New Zealand International	17 completed 12 current	$2.5-10m	47

The Australian Sarcoma Study Group (ASSG), which originated in 2008, is a co-operative group of clinicians sharing interest in undertaking basic, translational, clinical and supportive care research to develop and deliver treatments of sarcomas and related tumours to the Australian community and globally. This organisation provided infrastructure enabling collaboration between multidisciplinary teams and bringing together health professionals working on development of best treatments and care for sarcoma cancer sufferers.

The network is focused on initiation and maintenance of a national sarcoma research capability in Australia, formation of international clinical trials partnerships and effective collaborations across cancer research disciplines. The ASSG's efforts and investments in infrastructure resulted in establishment of the first Australian sarcoma database and biospecimen bank, which will ultimately lead to delivery of more effective treatment for patients and generate new insights into effective treatment regimes. This network successfully provides an integrative link between paediatric and adult sarcoma communities and enables partnership with the wider community.

Major Achievements

The sarcoma clinical guidelines published by the network in a wiki format through Cancer Council has become one of the major achievements of the network, which is aiming to continue adding further cohort specific sarcoma guidelines in a similar manner. Importantly, the ASSG has been playing a significant role in supporting Australian sarcoma research through the generous philanthropic donations and Sarcoma Research Grants awarded to a number of basic science projects and PhD scholars.

The group has been recognised for its input into the basic scientific research of the biochemical and genetic mechanisms an understanding of which is necessary to advance the development of new and more effective treatments for sarcomas. The ASSG undertakes extensive work in this area that has been highly regarded and has been supported by NHMRC grants.

The ASSG participated successfully in clinical trials initiated by commercial entities, international networks and by the networks' own investigators. The findings of the open-label, multicentre phase II study of Denosumab (AMG 162) in subjects with recurrent or unresectable Giant Cell Tumour of bone conducted by the network and published in Lancet Oncology, revealed clear activity of Denosumab and offered the first successful systemic intervention for patients with inoperable disease.

Australasian Society for Infectious Diseases Clinical Research Network

www.asid.net.au

Years	Members	Studies	Funding	Publications
6	Australia wide New Zealand	3 completed 8 current	$1-2.5m	$1-2.5m

The Australian Society for Infectious Diseases Clinical Research Network (ASID CRN) was formed in 2009 by a group of infectious diseases physicians interested in facilitating high quality, multi-centre, investigator-initiated studies. The network consists of highly experienced clinicians and researchers across Australia and New Zealand who are dedicated to improving patient care through the advancement of infectious diseases research and building an effective research network that rapidly responds to evolving infectious diseases threats. It strives to strengthen existing and build new collaborations with similar groups in Australia, New Zealand and overseas and increase the potential of infectious diseases research across Australasia by encouraging global collaborative projects.

The mission of the ASID CRN is to improve patient outcomes by generating high quality evidence through multi-centre collaborative research efforts in infectious diseases. The primary focus of the ASID CRN clinician-initiated research is to answer problems of direct clinical relevance actively contributing to design, conduct and publication of clinically relevant, evidence-based infectious diseases research. Additionally, the impact of clinician-focused research within the ASID CRN is aimed at improving direct patient outcomes, facilitating physician effectiveness and providing valuable cost-savings to the health care system.

A number of successful research Priority Working Groups have been established within the network. Such groups as Gram Negative Infections, Prosthetic joint Infections/Native Joint Infections, Staphylococcus aureus Bacteraemia, Opportunistic Infections, drug-resistant Tuberculosis and Encephalitis have been successful at providing focused and functional research outcomes.

Major Achievements

A prospective epidemiological study COOEE conducted by the network, which received internal funding as well as financial support from the Royal Brisbane and Womens's Hospital Foundation, investigated risk-factors for ESBL Escherichia coli in Australia and New Zealand. The findings of the study published in 2014 had profound impact on clinical practice and empiric prescribing for patients with sepsis suspected to be due to Escherichia coli.

Australasian Stroke Trials Network

www.astn.org.au

Years	Members	Studies	Funding	Publications
19	Australia Wide New Zealand International	40 published 35 current	>$50m	180+

The Australasian Stroke Trials Network (ASTN) established in 1996 is the key body in promoting, facilitating and coordinating both commercially-sponsored and investigator-initiated stroke trials in Australasia. This network , which comprises 35 centres located in Australia, New Zealand, Singapore and Hong Kong, facilitates the development of coordinated strategies for involvement of the Australasian Pacific region in International Stroke Trials. The ASTN was initially set up to follow the network concept developed in North America and Europe.

The ASTN Committee plays an important role in providing effective communication channels between local clinicians, research centres and pharmaceutical companies seeking opportunities to initiate new clinical trials in Australasia. It offers assistance to study sponsors in assessment of feasibility of conducting new studies in Australasian region through appropriate recruitment forecasts, review of study protocols, budgets and logistics in the context of current competing studies. Its intimate understanding of local capabilities facilitates early identification and strategic resolution of potential problems with ethical review, enabling effective scientific research and timely trial completion.

Major Achievements

During the last decade the ASTN has successfully led or participated in a number of large late phase clinical trials that have initiated major changes in clinical policy and practice for the treatments of stroke both in Australia and internationally. Examples include but are not limited to:

- CAVATAS: Carotid and Vertebral Artery Transluminal Angioplasty. International trial to determine safety and effectiveness of angioplasty compared to carotid endarterectomy or best medical treatment in patients with carotid or vertebral artery stenosis. Findings resulted in a major shift in patients' care leading to change in clinical guidelines in relation to the use of stents.
- ARCH: The Aortic Arch-Related Cerebral Hazard. Phase III trial was the first to compare two antithrombotic therapy strategies (aspirin plus clopidogrel) to anticoagulation (dose adjusted warfarin, target INR 2–3)) for secondary stroke prevention in patients with atherothrombosis of the aortic arch. Patients treated with aspirin plus clopidogrel had a significant reduction in vascular death compared with patients on warfarin. This trial provided the impetus for further trials to establish optimal prevention regimes in this cohort.
- Extend-IA: Extending time for Thrombolysis in Emergency Neurological Deficits – IntraArterial. A randomised trial of clot retrieval after intravenous thrombolysis in ischemic stroke. This recent trial showed 40% improvement in outcome and has already been incorporated into clinical practice guidelines.
- INTERACT2: Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial. A randomised trial to establish the effects of early intensive blood pressure lowering on death and disability in haemorrhage patients. Results from this trial appear in stroke guidelines and have shifted practice in patients with acute haemorrhagic stroke.

Australia & New Zealand Breast Cancer Trials Group

www.anzbctg.org

Years	Members	Studies	Funding	Publications
37	Australia wide New Zealand International	33 completed 35 current	>$50m	>900

The Australia and New Zealand Breast Cancer Trials Group (ANZBCTG) is the largest independent, oncology clinical trials research group in Australia and New Zealand. For more than 35 years, it has conducted clinical trials for the treatment, prevention and cure of breast cancer. Breast cancer research conducted in Australia, predominantly by the ANZBCTG, has contributed to the significant improvement in breast cancer related mortality that has occurred over the last thirty years.

The ANZBCTG research program involves multicentre national and international clinical trials and brings together over 700 researchers in 87 institutions throughout Australia and New Zealand. This collaboration facilitates the conduct of clinical research in many centres with a wide national geographical spread and ensures the efficient sharing of knowledge, expertise and resources. As a result of such teamwork the translation of research into improved patient outcomes is expedited. Collaborative group clinical research, led by academic clinicians is unique in its focus on answering the clinically important questions that translate into such improved outcomes for patients.

The contribution of ANZBCTG research to international consensus statements, treatment guidelines, meta-analyses and overviews, including in the breast cancer sphere, the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) or 'Oxford Overview', St Gallen Consensus Statements and Cochrane reviews optimises the translation of health and medical research into better health and wellbeing. The ANZBCTG has promoted the value of consumer involvement in clinical trials and established the Consumer Advisory Panel (CAP) in 1998, which has been widely applauded.

Major Achievements

The ANZBCTG has contributed directly to many of the most important advances in breast cancer: primary prevention trials, IBIS 1 (tamoxifen, placebo) and IBIS 2 (anastrozole, placebo, including a bone substudy); the first adjuvant aromatase inhibitor trials (ATAC, BIG 1-98, and IES), chemotherapy studies and one of the major adjuvant Herceptin trials (HERA). Trials include but are not limited to:

- The international study IBIS-I, which recruited 2,674 Australian and New Zealand participants, demonstrated that tamoxifen reduced risk of hormone receptor positive breast cancer by 34% with benefits continuing to be effective several years after completion of the treatment;
- The outcomes of the IBCSG 15-95 trial highlighted importance of the longer follow ups for understanding endocrine responsive breast cancer triggering a shift away from the dose-intense chemotherapy regimens requiring growth factor and stem cell support;
- According to the results of the ANZ 8101 randomized trial, intermittent chemotherapy, compared with continuous treatment, was not only optimal for management of patients with metastatic breast cancer with superior tumour control but also resulted in better quality of life.
- The ANZ 0001 study provided clear evidence that, compared to standard chemotherapy (CMF), administration of capecitabine, for which a favourable toxicity profile allowed longer duration of treatment, resulted in improved overall survival for women with metastatic breast cancer.

Australia & New Zealand Melanoma Trials Group

www.anzmtg.org

Years	Members	Studies	Funding	Publications
16	Australia wide New Zealand International	2 completed 18 current	$2.5-10m	28

Since its establishment in 1999, the main focus of the Australian and New Zealand Melanoma Trials Group (ANZMTG) has been related to skin cancers and melanoma. The network has recognised the need for central support of melanoma trials for investigators and consumers and has been actively involved in coordinating efforts of researchers, health care professionals and consumers in conducting high quality clinical research for melanoma control. Since its first successful project in designing and conducting the randomised Phase III trial in melanoma, that compared adjuvant radiotherapy to observation in patients with resected nodal disease, ANZMTG has been developing and conducting new clinical trial protocols and research projects.

This group is leading the national clinical research agenda in melanoma and strives to attain maximum efficiency via streamlined processes and procedures. Its efforts in building capacity through effective partnerships fosters collaboration and exchange of ideas bringing together researchers, clinicians, healthcare professionals and consumers with an interest in melanoma clinical trials. ANZMTG provides a single point of contact for investigators and sponsors undertaking melanoma trials in Australia and New Zealand. It supports the development of large-scale, multi-centre melanoma studies of clinical relevance and importance which would be difficult for any single centre to complete.

Major Achievements

The network had successfully collaborated with other large Australian networks, POCOG and TROG, delivering significant outcomes that are of importance not only for the patients in Australia but also worldwide. One of the significant achievements of the group was development of the new melanoma-specific Quality of Life assessment tool. The original concept and design of this questionnaire were based on the outcomes of the ANZMTG RP 01.09 project. Development of this instrument was also supported by the European Organisation for Research and Treatment of Cancer confirming its international significance.

The ANZMTG 01.02 phase III trial was aimed at investigating effectiveness of post-lymphadenectomy radiotherapy in the treatment of the patients with melanoma at high risk of further lymph-node field and distant recurrence. The findings of this trial, published in Lancet Oncology, in 2013 proved the benefit of radiotherapy in managing local recurrence of stage III melanoma. This crucial outcome will be reflected in the new national melanoma treatment guidelines that are currently under development and will result in impact on health practices in Australia.

Australia New Zealand Gynaecological Oncology Group

www.anzgog.org.au

Years	Members	Studies	Funding	Publications
15	Australia wide New Zealand International	14 completed 5 current	$14m	71+

The Australia New Zealand Gynaecological Oncology Group (ANZGOG), which was established in 2000, is a not-for-profit company limited by guarantee and a health promotion charity that fundraise in all states of Australia. ANZGOG encourages and facilitates high quality national and international collaborative research dedicated to gynaecological oncology such as ovarian, cervical, uterine, vulvar and vaginal cancers. It has contributed to the initiation and successful conduct of investigator-led multicentre clinical trials recruiting across more than 51 sites throughout Australia and New Zealand.

These trials and research activities provide the opportunity for women in Australia and New Zealand to participate in important clinical trials that are seeking new treatments that hold the promise of improving their outcomes. ANZGOG is striving to increase awareness of gynaecological cancers and their treatments by providing access to information, resources, education and support to cancer patients and their families.

The trials conducted by ANZGOG continue to deliver results that benefit treatment practices and outcomes for women with gynaecological cancers. ANZGOG successfully collaborates with more than 26 international clinical research organisations worldwide through its membership of the Gynecologic Cancer InterGroup (GCIG) though which it collaborates with similar networks in the US, UK, and Germany. In Australia, the network works closely with the NHMRC Clinical Trials Centre at the University of Sydney.

Major Achievements

One of the main achievements of ANZGOG is its ability to establish successful research relationships across the globe. Since the very beginning of the Group's existence, its research projects have been completed in collaboration with a number of large Australian and international research bodies. ANZGOG has led three important international trials including PARAGON which has recruited 97 participants from the UK and Belgium; OUTBACK which has recruited 459 participants in Canada, Saudi Arabia, Singapore and the USA; and the Symptom Benefit quality of life study which recruited 764 participants from Canada, Ireland, France, Germany, Italy, Sweden and Japan. All of these studies recruited well in Australia and New Zealand as well. ANZGOG also collaborates locally with other Australian networks including ANZUP, AGITG, TROG and PoCoG to achieve successful completion of its clinical trials.

Australian & New Zealand Children's Haematology/Oncology Group

www.anzchog.org

Years	Members	Studies	Funding	Publications
29	Australia wide New Zealand International	3 completed 11 current	$1-2.5m	10+

Since its establishment in 1986 the Australian and New Zealand Children's Haematology/Oncology Group (ANZCHOG) has been dedicated to improving outcomes for children with cancer through conducting clinical trials as an integrated component of routine healthcare delivery. It is a national multidisciplinary, cooperative network formed to provide the infrastructure for collaboration of professionals working in the fields of paediatric blood diseases and cancer. It is an independent non-profit organisation with a multi-disciplinary membership involved in national and international clinical trials, clinical and laboratory based research. It also holds workshops, seminars and an annual scientific meeting.

The vision of this group is to ensure that all children and adolescents with cancer and associated blood diseases are provided with the highest quality evidence-based care to ensure optimal outcomes in terms of survivorship and quality of life.

The ANZCHOG upholds core values of excellence, compassion, commitment and collaboration and its research activities underpinned by evidence-based practice adherence to the high ethical standards. The primary purpose of the work conducted by the ANZCHOG is the best practice and innovation through quality research by means of the paediatric cancer clinical trials leading to improved outcomes for children and adolescents with cancer and blood diseases. The clinical trials conducted by the group are vital for improvements in the cure, treatment and care of Australian and New Zealand children with cancer.

Major Achievements

The network has successfully completed 3, and is currently conducting 11 studies, one of which is a large multicentre trial, IntReALL 2010, initiated by an international network and supported by funding from the NHMRC.

The findings of the International Collaborative Trial for Relapsed and Refractory Acute Lymphoblastic Leukaemia (UKALLR3) conducted by the network and published in 2010 in the Lancet had profound effect on clinical practice providing scientific grounds for elimination of inferior cancer treatments.

Australian & New Zealand College of Anaesthetists Clinical Trials Network

www.anzca.edu.au/ctn

Years	Members	Studies	Funding	Publications
12	Australia wide New Zealand International	14 completed 14 current	$25-50m	30+

The Australian and New Zealand College of Anaesthetists Clinical Trials Network (ANZCA CTN), which was established in 2002 (as the ANZCA Trials Group), has been conducting practice changing NHMRC-funded multicentre trials for almost a decade. The ANZCA CTN is committed to providing evidence-based practices in anaesthesia, pain and perioperative medicine.

In 2009 a Memorandum of Understanding between the College and Monash University marked its co-location at the University's School of Public Health and Preventive Medicine. Its has developed sustainable network infrastructure, strengthened by engagement with a range of stakeholders and has been supported with over $25 million in total research funding. It is capable of achieving its ambition of becoming a world leader in delivering high quality trial evidence that is translated into safe and effective practice.

The primary goal of the network is to improve the evidence base of anaesthesia by endorsing high quality, multicentre randomised controlled trials and related research.

The ANZCA members are highly skilled in the theory and practice of research methodology and have a record of success in co-ordination, conduct and management of large multicentre randomised controlled trials. The ANZCA CTN also provides research infrastructure support for Fellows and trainees of the College for survey research purposes and administers the Pilot Grant Scheme.

The network has also developed a business case for the employment of anaesthesia research co-ordinators in network hospitals. It manages several large multicentre randomised trials in conjunction with collaborative centres in Australia, New Zealand and abroad and has also been responsible for multicentre observational studies and surveys such as the Australasian Obstetric General Anaesthesia for Caesarean Section Survey and the Research into Elderly Patient Anaesthesia and Surgery Outcome Numbers Audit.

Major Achievements

In 1995 the ANZCA investigators initiated its first randomised, international, multi-centre trial, which also attracted NHMRC funding: The Multicentre Australian Study of Epidural Anaesthesia and Analgesia in Major Surgery(MASTER Trial) was published in the Lancet in 2002, the RELIEF Trial conducted by the network in 2012 attracted the highest ranked NHMRC Project grant, and in 2015 the highest value NHMRC Project grant was allocated to the PADDI trial.

Australian & New Zealand Intensive Care Society Clinical Trials Group

www.anzics.com.au

Years	Members	Studies	Funding	Publications
21	Australia Wide New Zealand International	41 completed 48 current	>$50m	130+

The Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS CTG) was established in 1994. What started as a small group of professionals, committed to seeking better clinical research and greater quality evidence in intensive care medicine, has evolved into a group with more than 500 members who are world leaders in the design and conduct of multicentre trials that define best treatment for patients with immediately life-threatening critical illness. The network is active in more than 90 adult and paediatric Intensive Care Units (ICUs) and interacts closely with the registries that are maintained by the ANZICS Centre for Outcome and Resource Evaluation.

The ANZICS CTG is a highly skilled and collegial community of clinicians and researchers dedicated to generating new evidence to guide treatment and improve outcomes for patients who are treated in an ICU. to intensive care. Its mission is to promote excellence in Intensive Care medicine through collaborative clinical research focused on improving patient-centred outcomes, by the conduct of multi-disciplinary and international research collaboration that results in the delivery of high-quality programs of research that address clinically relevant questions. The ANZICS Clinical Trials Group is a standing committee of the Australian and New Zealand Intensive Care Society (ANZICS).

Major Achievements

The ANZICS CTG has regularly published practice changing clinical trials in high impact general medical journals including more than 10 publications in the NEJM. The SAFE study demonstrated that cheap saline fluid was as effective as expensive albumin for most patients and actually superior for patients with traumatic brain injuries. The DECRA study showed that a widely implemented treatment, decompressive craniectomy for patients with severe diffuse brain injury, was harmful and should be abandoned. The NICE-SUGAR study demonstrated, unexpectedly, that the use of insulin to achieve tight control of patients' blood glucose levels resulted in higher mortality. The ARISE study demonstrated that a labour and resource intensive strategy for resuscitation of patients with septic shock was no better than standard approaches. The CHEST study demonstrated that an expensive intravenous fluid more frequently resulted in renal failure requiring dialysis therapy and that the fluid should not be used.

The results of all of these studies have been incorporated into international guidelines and have contributed to the substantial improvements in mortality for patients treated in ICUs that has been observed in Australia in the last decade. Observational studies conducted by the ANZICS CTG during the 2009 influenza pandemic were also influential in definitively establishing the severity and impact on healthcare services of the newly emerged virus.

Australian & New Zealand Urogenital & Prostate Cancer Trials Group

www.anzup.org.au

Years	Members	Studies	Funding	Publications
7	Australia wide New Zealand International	6 completed 14 current	$18m	17

The Australian and New Zealand Urogenital and Prostate Canter Trials Group (ANZUP) is an active cancer cooperative clinical trials group, established to bring together all the professional disciplines and groups involved in researching and treating prostate and other urogenital cancers. ANZUP was established in 2008 for the purpose of conducting national and international research in these cancers. The group's focus is on the conduct of clinical trials to improve the treatment of Bladder, Kidney, Testicular and Prostate Cancers for all appropriate patients in Australia and New Zealand. Its collaboration with various professionals across multiple disciplines provides numerous opportunities for streamlined clinical research of the highest quality for the benefits of patients with urogenital cancers.

ANZUP has built an impressive multidisciplinary membership while developing strong relationships with other national groups like the Prostate Cancer Foundation of Australia, Cancer Councils, other the national cancer cooperative trials groups, COSA, Kidney Health Australia as well as Australian Government, industry and other non-government organisations. ANZUP also works closely with its Consumer Advisory Panel to achieve better understanding of consumer and community perspective on issues related to their clinical trials. This also ensures that the results of the research are communicated back to the community clearly and often, and that the community has the opportunity to engage in and promote this type of research.

Major Achievements

ANZUP has successfully led or participated in a number of studies leading to changes in Australian healthcare practice. Examples include a prospective cohort study investigating the effects of testosterone deficiency on quality of life in testicular cancer survivors which deepened the understanding of the risks of androgen deficiency and instigated appropriate testing and hormone replacement therapy; a study of the long-term psychological sequelae of surviving testicular cancer which highlighted the importance of appropriate screening and multidisciplinary involvement; a study of management patterns amongst medical oncologists which endorsed increased surveillance for patients with stage I seminoma or non-seminoma; and a phase II trial (EVERSUN) that confirmed the feasibility and safety of Everolimus alternated with Sunitinib in patients with advanced renal cell carcinoma but recommended current practice shouldn't change.

The recently completed exploratory investigation 'Sexual Wellbeing and Quality of Life after Prostate Cancer in Gay and Bisexual Men and their Partners' will provide evidence-based recommendations for health professionals for culturally appropriate supportive care interventions. The network also completed the accelerated BEP Phase II and initiated the accelerated BEP Phase III study comparing accelerated versus standard BEP chemotherapy in patients with intermediate and poor-risk metastatic germ cell tumours; completed a randomised controlled trial of a mindfulness-based cognitive group intervention to reduce psychological distress in men with advanced prostate cancer; completed an observational study 'Chemotherapy and Cognition', and has ongoing participation in an international phase III randomised SORCE trial comparing effects of Sorafenib versus placebo in patients with resected primary renal cell carcinoma.

Australian Epilepsy Clinical Trials Network

www.neurotrialsaustralia.com/strategic-alliances/epilepsy

Years	Members	Studies	Funding	Publications
2	Australia Wide	3 current	$1-2.5m	N/A

The Australian Epilepsy Clinical Trials Network (AECTN) was established in 2013 as a coordinating body for epilepsy clinical trial centres in Australia and New Zealand in order to facilitate both industry-funded and investigator driven research. It is a part of the Neuroscience Trials strategic alliance representing professional network of clinicians and other healthcare professionals committed to seeking improvement in treatment of Epilepsy and related disorders through the cooperative planning, implementation, analysis and reporting of controlled clinical trials and of other relevant research.

AECTN has already attracted significant industrial funding and has initiated and commences recruitment into multicentre clinical trials investigating anti-epileptic treatments, one of which is in collaboration with Northeast Regional Epilepsy Group (USA). Another trial, which received funding from Upsher-Smith Laboratories, is currently under development and will be examining safety and efficacy of Midazolam Intranasal Spray (USL261) for the treatment of intermittent bouts of increased seizure activity.

Major Achievements

Whilst this network is comparatively new, it has already managed to provide a crucial link and become the central point of contact for industry and epilepsy researchers in Australia.

Australian Musculoskeletal Clinical Trials Group

www.anzmusc.org

Years	Members	Studies	Funding	Publications
1	Australia wide New Zealand	1 Completed	$29,500	1

The Australia & New Zealand Musculoskeletal (ANZMUSC) Clinical Trials Network is a newly established group, formed to optimise musculoskeletal health through high quality, collaborative clinical research. The focus is on all forms of arthritis and musculoskeletal conditions including osteoarthritis, rheumatoid arthritis, osteoporosis, trauma and regional conditions (such as low back pain, neck pain, and shoulder pain).

The vision, mission and values of the group were established at the inaugural summit of the network, which took place April 2015. A caretaker steering committee, comprising multidisciplinary clinician-researchers from Melbourne, Sydney, Adelaide and Wellington, New Zealand, and a consumer representative was also ratified. One-year goals include defining a clear structure and governance, key functions and membership structure, and securing infrastructure support. The strong support expressed at the summit across a wide breadth of stakeholders indicates that the network is likely to become truly international in the foreseeable future.

Major Achievements

The highly successful first ANZMUSC Summit was supported by consumer organisations (Arthritis Australia, Arthritis and Osteoporosis Victoria, Arthritis South Australia, Arthritis and Osteoporosis Tasmania), professional societies (Australian Orthopaedic Association, Australian Physiotherapy Association, Australian Rheumatology Association), Monash University and Cabrini Health. It was attended by 100 participants affiliated with 22 universities across Australia and New Zealand, as well as various research institutes and hospitals, consumer organisations, professional societies, NHMRC, State Departments of Health, Australian Commission on Quality and Safety in Health Care and health insurers.

A review of the current scope of musculoskeletal trials in Australia, published in the Med J Aust in 2014 indicated that these conditions receive relatively less research focus compared to other less costly and less prevalent health priorities. There was also a scarcity of high-quality research focused upon closing well-recognised evidence and evidence-practice gaps indicating the need to ensure that clinical research in this field is strategic and of high impact.

A survey conducted in 2015 involving 112 ANZMUSC trialists across a wide array of disciplines indicated a wide variety of potential benefits of ANZMUSC membership which could be summarised into six themes: collaboration/networking; funding; learning/gaining experience/peer review; priority setting; advocacy for musculoskeletal disease/research; and avoidance of duplication.

Australian Paediatric Research Network

www.aprn.org.au

Years	Members	Studies	Funding	Publications
7	Australia Wide	2 current	$500,000-1m	14

The Australian Paediatric Research Network (APRN) was founded in 2007 and is the first of its kind in Australian, as a network focused on the field of general paediatrics. It represents a collaborative body of researchers keen to contribute to new research as well as to further existing investigations relevant to both public and private practice. It has a unique ability to develop research capacity by involving clinicians in research activities and enhancing recruitment for community based research projects. More than 500 active members of the network are dispersed widely throughout Australia.

In 2013, the network was awarded its first NHMRC project grant for the randomised clinical trial "Impact of a sleep intervention in Attention Deficit Hyperactivity Disorder (ADHD): translational randomised trial", which is currently under way and is aiming to recruit 476 participants. Projects proposed by APRN members include the "Parent needs around Autistic Spectrum Disorders diagnosis", "Paediatric action on food allergy", "Australian paediatric ADHD study" and "Adolescent girls with ADHD study".

A number of supplementary materials such as "How to conduct research" and "Translation Toolkit" have been developed by the network to assist paediatricians and researchers in developing and conducting quality research projects from beginning to end. All these resources are made available not only on the network's website, but can also be found on the Royal Australian College of Physicians, The Royal Children's Hospital and Murdoch Children Research Institute websites thereby assisting in producing high quality clinical research evidence and timely delivery of treatments.

Major Achievements

In order to ascertain the clinical research priorities of its members, the APRN conducted Delphi surveys in 2007 and 2014. In addition, three multi-topic surveys were carried out between 2010 and 2013 assessing practice of the network members' across a variety of child health conditions. APRN successfully conducted two national, clinical practice audits in 2008 and 2013 – highlighting that the case load resulting from developmental and behavioural disorders was substantial and that there was substantial variation between paediatricians in prescribing and diagnostic practices.

Australian Primary Care Research Network

www.apcren.org.au

Years	Members	Studies	Funding	Publications
2	Australia wide	N/A	$50,000-100,000	N/A

Since its recent establishment in 2013, the Australian Primary Care Research Network (APCReN), which is hosted in the General Practice and Primary Health Care Academic Centre at the University of Melbourne, stands as a national support service for Practice-Based Research Networks (PBRNs) across Australia. This network supports research activities by sharing its knowledge and resources. It actively creates linkages between existing PBRNs as well as providing advocacy and support for the new PBRNs across Australia.

The APCEeN provides communication and collaboration between affiliated Universities and other relevant bodies, recruitment of practices or health professionals for research projects and advice on conducting research in primary care. Most of the research involving patients, practitioners or system happens within the community settings and is logistically challenging. APCReN aims facilitate overcoming these difficulties by providing infrastructure to support practice-based research and generate consistent data relevant to both clinical practice and health policy.

Major Achievements

The APCReN's success in bringing together primary care networks, mapping out cost mechanisms and assessing resource requirements for multi-site primary care trials indicates that this model of interaction has potential of being used to assist the conduct of studies and facilitate successful funding applications.

Cooperative Trials Group for Neuro-Oncology

www.cogno.org.au

Years	Members	Studies	Funding	Publications
7	Australia wide New Zealand International	4 completed 9 current	Not Available	4

The Cooperative Trials Group for Neuro-Oncology (COGNO) was established in 2007, following identification of the need to develop a central mechanism enabling a coordinated, structured approach to the management of large scale multi-centre neuro-oncology trials in Australia. The group is focused on conducting investigator-initiated collaborative trials addressing important clinical questions in patients with brain tumours. It strives to achieve better health outcomes for patients and those affected by brain tumours through clinical trials research.

This group is a member of the Cooperative Clinical Trials Groups of the Clinical Oncological Society of Australia (COSA) and formed a close working relationship with the COSA Neuro-Oncology Group.

COGNO's research activities have been funded by Cancer Australia and the Cancer Institute NSW and the group's clinical trials activities have been coordinated by the NHMRC CTC located at the University of Sydney. COGNO's membership continues to increase with there being 428 members currently, including members located in New Zealand, Singapore, Canada, Ireland, India, Sweden and USA. The group also has consumers and industry associate members. The COGNO's Annual Scientific Meetings had been hugely successful in bringing together professionals from all over the world.

COGNO has successfully conducted two "Ideas Generation Workshops', where a number of novel ideas and concepts were discussed and it is anticipated that some of these will be developed and submitted for consideration and review by COGNO Scientific Advisory Committee. It's been seeking new trial opportunities and the group has been considered as an important contributor to neuro-oncology clinical trials by the large research groups such as EORTC, NCIC and the US groups.

Major Achievements

One of the important contributions of the network was the first Australia-wide study of patterns of care in neuro-oncology. A questionnaire was used to assess neuro-oncology services, treatment protocols and patterns of supportive care at 28 Australian cancer centres that are involved in the management of glioblastoma. The findings of this study helped identify potential targets for future clinical trials and areas for education to encourage clinicians comply with treatment guidelines.

COGNO's clinical trial portfolio is increasing and has achieved meaningful outcomes. In particular, COGNO collaborated with the EORTC to bring the important CATNON trial to Australian sites with excellent trial accrual. The Australia based CABARET trial has achieved international prominence and will likely change international clinical practice. Finally, COGNO's involvement in two randomised multi-site Phase II clinical trials VERTU and ACED has been announced recently and these trials are currently under development.

Multiple Sclerosis Research Australia Clinical Trials Network

www.mstrials.org.au

Years	Members	Studies	Funding	Publications
5	Australia wide New Zealand	1 current	$2.5-10m	N/A

The Multiple Sclerosis Research Australia Clinical Trials Network (MSRACTN) was established in 2010 in order to facilitate clinical trials for Multiple Sclerosis in Australia and New Zealand. The network aims to increase awareness of and access to clinical trials for patients with this complex and often disabling disease that is characterised by variable and unpredictable progression. Modelled on other successful clinical trials networks, the focus of the group's activity remains improvement of the opportunity to participate in trials for patients.

A key role of the CTN is facilitating easy access to information on clinical research for patients with aim of enhancing trial recruitment. The group also aims to facilitate interaction between trial sponsors, trial sites and the community.

The MSRACTN provides assistance with both industry-sponsored and investigator-initiated studies and informs trial sponsors about capacity of different sites and institutions to undertake trials throughout Australia and New Zealand. The network provides a protocol review service to investigator-led trials and small biotech sponsors in the region. The Executive Members of the Network serve on the advisory boards for a number of commercial trials and are directly involved in coordination of a single clinical trial.

Major Achievements

The network is currently involved in the PrevANZ trial, which is a result of collaborative efforts between the MSRACTN and Neuroscience Trials Australia. This Phase IIb Randomized, Double-Blind, Placebo-Controlled, Dose Ranging Trial is designed to determine the safety and efficacy of Vitamin D3 in preventing progression of disease in patients with a first demyelinating event. The trial is open to recruitment currently and aims to recruit 240 participants. It was initiated by the network's own investigators and has received $2,800,000 funding from Multiple Sclerosis Research Australia via donations from state based multiple sclerosis charities, Trish MS Research Foundation, Foundation 5 Million and the John T Reid Trust.

NSW Better Treatments 4 Kids

www.bt4k.com.au

Years	Members	Studies	Funding	Publications
5	NSW	N/A	$250,000-500,000	N/A

The formation of NSW Better Treatments 4 Kids (BT4K) in 2010 was made possible with the funding from the Office for Health and Medical Research within NSW Health. BT4K is a collaboration of paediatric researchers and health professionals located at children's hospitals and research institutes with a common interest in clinical trials. The current member sites of BT4K are Sydney Children's Hospital, Randwick and the Children's Hospital at Westmead, as well as John Hunter Children's Hospital in Newcastle. Sydney Children's Hospital Network hosts the group's Secretariat.

The network aims to improve health outcomes of children and their families by increasing the quantity and quality quantity of paediatric clinical research and by promoting evidence-based health care. It is focused on promoting paediatric clinical research that meets and exceeds international standards of ethical practice and good clinical practice, engaging parents and families as active research partners.

Whilst the BT4K is a relatively new organisation, its short existence had been marked by successful participation in a number of initiatives such as delivery educational programs for researchers along with provision of advocacy and links with commercial entities. Its major emphasis to date has been to engage with consumers to achieve interest and involvement in clinical trial development.

Major Achievements

BT4K launched its website and Twitter feed (@BT4K_NSW) in 2014 with the objective being to raise public awareness and increase impact of on consumers and researchers and these provide information about network-related activities. The network conducts training and education workshops that are designed to increase consumer awareness of the processes associated with conducting clinical trials and research in general. The 'Consumer Participation in Research' workshops are conducted at no cost to attendees.

The 'Parents and Caregivers Research Workshop' provides information on research related topics such as funding and ethics processes, data linkage, research terminology and tips on contributing effectively to a research team. Another important workshop 'Involving Consumers in Research, Clinician/Researcher' offered modules about foundations, principles, barriers and methods of the research.

Paediatric Research in Emergency Departments International Collaborative

www.predict.org.au

Years	Members	Studies	Funding	Publications
11	Australia wide New Zealand	16 completed 17 current	$2.5-10m	24

The Paediatric Research in Emergency Departments International Collaborative (PREDICT) is a research network bringing together research institutions, healthcare providers and researchers involved in paediatric emergency care across Australia and New Zealand. It is the largest paediatric emergency medicine research network in the southern hemisphere. PREDICT includes 15 sites across Australia and New Zealand (including all tertiary paediatric emergency departments), comprises multidisciplinary teams undertaking multicentre paediatric emergency research projects, facilitates professional development of members providing opportunities for higher degrees and provision of post-doctoral mentoring, provides research training and facilitates collaboration with global paediatric emergency medicine networks.

PREDICT was recently awarded a Centre for Research Excellence grant from the NHMRC (2014-2018). PREDICT aims to establish an evidence base and improve emergency care for children and adolescents through rigorous research by coordinating research activities among participating institutions and providing sustainable research infrastructure. The strength of the network lies in the conduct of high quality research that is driven by clinicians who are empowered to lead clinical change and are viewed by peers as setting the standards for clinical care.

A key feature in its success has been the development of close collaborations with Australian and international organisations. PREDICT has formed a successful ongoing partnerships with international paediatric emergency medicine research networks from the USA, Europe, UK and Canada including the formation of the global Paediatric Emergency Research Network (PERN). In Australia, PREDICT has established linkages with the Murdoch Childrens Research Institute (MCRI), National Trauma Research Institute in Melbourne, Neurosurgery at Austin Heath in Melbourne, the Paediatric Emergency Medicine Society (PEMS), Royal Australian College of Physicians (RACP), Australasian College for Emergency Medicine (ACEM), and the Advanced Paediatric Life Support course (APLS).

Major Achievements

The group has conducted a randomised trial that compared intravenous with nasogastric hydration in infants admitted with bronchiolitis and the results of this trial are now translated into clinical practice in Australasia and internationally. A retrospective Case-Control study, "Predictors of Severe H1N1 Infection in Children Presenting with Influenza Like Illness," was initiated by the international network (PERN) and led by PREDICT.

The study has identified robust, generalizable, and independent risk factors that can be used to identify children who are at higher risk of severe outcomes when presenting with influenza like illness.

Paediatric Trials Network Australia

www.bt4k.com.au

Years	Members	Studies	Funding	Publications
4	Australia wide	18 current	$1-2.5m	N/A

The Paediatric Trials Network Australia (PTNA) founded in 2011 and draws together paediatric researchers from around the country who have the aim of improving child health through the facilitation of paediatric clinical trials. It is a not-for-profit, virtual and inclusive network that is open for membership to any paediatric research organisation or individual dedicated to increasing the quality and quantity of paediatric research in Australia. Rather than duplicate the effort of other established paediatric research networks, the PTNA hopes its infrastructure and advocacy efforts can complement the activity of other networks and benefit all paediatric researchers, and ultimately Australian children.

The PTNA is focusing on the conduct of multi-centre paediatric studies developed by investigators or by industry partners across all therapeutic areas. This may include randomised controlled trials with drugs, devices or other health interventions, as well as observational and health services research. The PTNA facilitates access to a critical mass of researchers and enough volunteers across the country that clinical trials can be completed successfully, as well as provide infrastructure for increasing and accelerating communication and data collection across the country.

The PTNA provides a platform for advocacy for collaborative clinical research for paediatrics in Australia, improving the Australian operating environment for paediatric clinical trials sponsored by industry, increasing quality and quantity of investigator-driven paediatric trials and strengthening the evidence base for the treatment of all children and adolescents. Network member institutions and researchers are committed to promotion of high quality and efficient multi-centre collaborative clinical trials and optimising effective delivery of health care by influencing policies, procedures and translation of research into practice.

Major Achievements

The network had received a federal grant as part of the National Collaborative Research Infrastructure Strategy, which resulted in the successful development of the Clinical Trials Data Management Software (CTDMS) system. This was launched in late 2013 under the name of WebSpirit and is utilised by a number of trials across Australia, with a combined sample size of more than 4,000 participants. This data management system provides an affordable, regulatory compliant, option for data management to Australian paediatric clinical trial teams running investigator initiated clinical trials. Investigators from PTNA member institutions are able to utilise the system via a discounted per project but the system is also available to non-PTNA member institutions.

Palliative Care Clinical Studies Collaborative

www.caresearch.com.au

Years	Members	Studies	Funding	Publications
9	Australia wide International	37 completed 12 current	$10-25m	100+

Since its establishment in 2006, the major objective of the Palliative Care Clinical Studies Collaborative (PaCCSC) has been generation of the high quality research, to underpin the evidence base for optimal end-of-life care. This has included the development and evaluation of medicines as well as other interventions for improved management and alleviation of multiple associated symptoms including pain, confusion, breathlessness, and gastrointestinal symptoms. The network maintains a central coordinating office in Adelaide with participating hospitals and health services located throughout Australia. Clinical studies conducted by PaCCSC have directly benefited patients and been incorporated into best practice in Australia and internationally. The group was formed following recognition that many treatments used commonly at the end of life to assist with managing or alleviating patients' symptoms had little or no evidence to support their use.

The Collaborative has an increasing the number of sites that are participating in Phase III and Phase IV studies. Under the current funding agreement with the Commonwealth the PaCCSC will complete a further four Phase III studies and continue to build relationships with national and international stakeholders and collaborators. The PaCCSC is also conducting multiple other trials that have been supported by competitive grant funding.

Major Achievements

The PaCCSC is recognised for its global leadership of clinical trials in the field of palliative care. The structure and processes of PaCCSC have been adopted by multiple research networks with the same objectives in a range of countries including Japan and the United States. Since its establishment various national and prestigious international awards bestowed on individual PaCCSC members.

The group has conducted multiple trials, many published in high impact general medical journals, that have improved the practice of palliative care and have been adopted in international guidelines for the management and alleviation of symptoms including pain, breathlessness, and gastrointestinal symptoms.

Primary Care Collaborative Cancer Clinical Trial Group

www.pc4tg.com.au

Years	Members	Studies	Funding	Publications
6	Australia wide New Zealand International	19 completed 17 current	$10.6m	75

The Primary Care Collaborative Cancer Clinical Trials Group (PC4) was established in February 2009, with support from Cancer Australia, to promote the conduct of high quality cancer research in primary care. The vision of the Group is to prevent cancer, to improve care and outcomes for people affected by cancer, to influence health care policy, and to promote best practice cancer care. This is done by fostering collaboration among researchers, health professionals and consumers; building research capacity through Training Awards, Concept Development and other workshops, and mentoring early career researchers; and facilitating the conduct of high quality research by providing our trial coordinators with resources tailored to complex intervention trials.

The expertise of our members covers all aspects of the cancer continuum from prevention, screening and early detection, to survivorship and palliative care. The community perspective is integrated into all activities by members of a Joint Community Advisory Group and a Consumer Link Register.

Major Achievements

The group's largest study, Which test is best?, was a randomised controlled trial of a consumer-oriented familial cancer risk tool on risk-appropriate colorectal cancer screening. The trial demonstrates the potential power of research in primary care with participation of 2025 people (with a completion rate of 88 per cent) involving 55 general practices in Melbourne and Sydney. The findings of the ProCare trial revealed that shared care for prostate cancer is acceptable, safe and cost-effective, and have contributed to the evidence base for future models of care for cancer survivors.

The Molemate trial demonstrated that using new and expensive technology (a hand-held scanner) was no more effective at improving the diagnosis of melanoma in primary care than implementing the existing 7-point checklist, which has now been integrated into several GP software systems. PC4-supported economic modelling research on the role of genetic testing in risk-stratified prostate cancer testing and established the present lack of evidence to warrant the use of existing genomic profiling for population stratification.

The PC4 phase II trial of acupuncture for lymphoedema in breast cancer demonstrated the safety and acceptability of this technique and is an important prelude to further clinical efficacy trials. The breadth of PC4-supported research is further demonstrated in the group's current portfolio - the development of risk assessment tools to support tailored cancer screening, an intervention to promote earlier symptomatic presentation in patients at high risk of lung cancer, a model of survivorship care for haematology patients, and a project to identify what patients want from their GPs for end-of-life care.

The group consider that one of its major achievements is its engagement with consumers through the establishment of a Joint Community Advisory Group (JCAG). Members with diverse cancer experiences and location were recruited through an innovative national open call for expressions of interest. PC4 provides a mechanism for them to support each other with a semi-structured Peer Support Program, with members paired to communicate at least monthly, and opportunities to participate in all PC4 activities are shared according to interest and availability.

Psycho-Oncology Co-operative Research Group

www.pocog.org.au

Years	Members	Studies	Funding	Publications
10	Australia Wide New Zealand International	18 completed 44 current	$2.5-10m	30+

The Psycho-Oncology Co-operative Research Group (PoCoG) was established in 2005 in response to a recognised need to develop the capacity and co-ordinated collaboration to conduct large-scale, multi-centre psycho-oncology and supportive care research. The research interests of the group are focused on the area of Psycho-Oncology, investigating psychological, social and emotional issues, quality of life, supportive care needs, processes of decision-making and communication between patients and carers affected by cancer and health professionals.

The main office is located at the School of Psychology, University of Sydney with the majority of its 1,382 active members being located in Australia (with some associate members located in New Zealand and internationally). This large network is actively involved in the Cooperative Clinical Trials Groups of the Clinical Oncological Society of Australia. It is jointly funded by Cancer Australia and the Cancer Institute NSW. PoCoG is recognised as a leader in the field and regarded internationally for excellence in Psycho-oncology research combined with effective and continuing leadership. The Scientific Advisory Committee of the network is responsible for strategic direction, research priorities, scientific rigour and standards of the network studies.

Major Achievements

Over the 10 years of its existence, this group has created a large body of research completing 18 studies, some of which has reflected collaborative efforts with the ANZBCTG, the ANZUP, the ANZGOG, the TROG, and the PC4, as well as the Queensland Institute of Medical Research, and the Queensland University of Technology Treatment Focused Genetic Testing Collaborative Group. At present, there are a 44 active studies conducted by the network members, which reflects extensive support of the network by different government, commercial and private bodies. The network promotes the generation of feedback from a range of professionals with the aim being to develop research studies that are relevant to clinicians and patients. Focus groups consisting of psychologists, social workers, nurses and other health professionals working with cancer patients have been conducted across Australia to elicit feedback about priority areas for research in psycho-oncology. A large proportion of the group members (61%) participated in this 6-weeks project in 2008 via face-to-face meetings or teleconference by an independent facilitator. The results were used to construct a quantitative questionnaire to identify key research priorities and needs among health and research professionals in psycho-oncology in order to guide the development of large multicentre clinically relevant studies in psycho-oncology.

The group conducts two Concept Development Workshops a year to allow network members to obtain expert feedback on a research concept to develop it to the stage of grant submission. PoCoG has also developed a range of resources to support Psycho-Oncology researchers, including a searchable database of Psycho-Oncology Patient Reported Outcomes, Standard Operating Procedures for all phases of research in the field, statistical consulting services and a Quality of Life office.

The Australasian Consortium of Centres for Clinical Cognitive Research

www.neurotrialsaustralia.com/strategic-alliances/dementia-ac4r

Years	Members	Studies	Funding	Publications
14	Australia wide New Zealand International	2 completed 13 current	$2.5-10m	5

The Australasian Consortium of Centres for Clinical Cognitive Research (A4CR) was officially established in 2000 although an informal consortium had been in existence since 1994. The AC4R has grown to be a successful network bringing together all centres that are involved in clinical research of Alzheimer's disease and other dementias throughout Australasia. It has substantial experience in the conduct of phase II, III and IV clinical studies and provides a professional interface between industry and clinical investigators involved in cognitive research.

At the start of 2012 the AC4R comprised more than 140 leading academic clinicians specialising in geriatric medicine, neurology, psychiatry, psychopharmacology, psychogeriatrics, neurobiology, nuclear medicine, and neuropathology. The AC4R aims to facilitate collaborative clinical cognitive research in Australasia, establish a forum for the exchange of information relevant to research in cognitive disorders, consider and make recommendations upon methodologies of clinical cognitive research and to advocate for appropriate treatment of clinical cognitive disorders.

The creation of the AC4R coincided with a series of significant changes in the care of patients with dementia, including the establishment of specialised memory clinics, improved methods for assessing people with dementia, improved opportunities for participation in clinical trials for Alzheimer's disease and other dementias, and the development of the screening methodologies.

Major Achievements

The AC4R had successfully participated in a number of large Phase II-IV international multi-centre trials initiated by international networks and funded by the large pharmaceutical companies such as Eli Lilly, Sanofi-Aventis, Hoffman-La Roche, Eisai Ltd, GlaxoSmithKline, Pfizer Inc. and Novartis. The phase III trial IDENTITY, which recruited over a 1000 participants across the globe and investigated the effect of -Secretase inhibition on the progression of Alzheimer's disease, provided an important step in understanding of disease progression and its mechanisms.

Currently the AC4R is participating in 13 international multicentre trials that are at the different stages of the development. Also the group is working on a number of the manuscripts reporting the results of the latest studies investigating the role of various treatments in alleviating the symptoms of Alzheimer's type of dementias, which will further research in this area and provide the evidence base for the future studies.

The Australasian Kidney Trials Network

www.aktn.org.au

Years	Members	Studies	Funding	Publications
10	Australia Wide	3 completed 5 current	$10-25m	58

Following the IDEAL trial, the imperative for a clinical trials network in the area of kidney disease was identified by the Australian and New Zealand Society of Nephrology (ANZSN) so as to address the lack of infrastructure to support locally coordinated, multi-centre, investigator-initiated clinical trials in kidney disease. In late 2003 the ANZSN council asked for expressions of interest to form a network, and in 2004 the proposal for the Australasian Kidney Trials Network (AKTN) with a Brisbane-based Operations Secretariat was endorsed by ANZSN. Together with the ANZSN, Kidney Health Australia (KHA) provided seed funding, which was leveraged to obtain an NHMRC Enabling Grant and in 2005 the AKTN commenced operations. Since then a group of national leaders in nephrology, representing geographically diverse locations and special interests have cooperated in establishing a successful, world-class research network. Over the past 10 years the AKTN has accumulated a critical mass of research enabling expertise under a unique and unrivalled operational structure.

The mission of the AKTN is to deliver high quality clinical trials to improve the health and wellbeing of people with kidney disease. To achieve this, the AKTN in conjunction with global collaborators including the European Vasculitis Study Group (EUVAS) and the Canadian Kidney Knowledge Translation and Generation Network (CANN.NET) designs, conducts and supports clinical trials in Australia and New Zealand (ANZ) thereby enabling a broad range of research concerned with the prevention and treatment of kidney disease. The AKTN is also committed to fostering clinical trials expertise in ANZ and the Asia Pacific region by offering formal educational and training opportunities (higher research degree scholarships and fellowships) along with informal learning opportunities (mentoring early career researchers; research resource and knowledge sharing). Representation on AKTN's scientific committee, trial management committees and special interest groups by members of the kidney care community including patients, nurses, dietitians and other allied health professionals, ensures the AKTN retains a relevant and wide-reaching research perspective with a firm focus on patient-centred outcomes.

Major Achievements

Chronic kidney disease (CKD) is a major public health problem in Australia and the world. Despite this burden of disease, the speciality of Nephrology is under-represented in published clinical trials, being the lowest of any internal medicine speciality. The AKTN provides the infrastructure to increase research in kidney disease by providing support to clinical researchers with a clinical trial concept but without the experience or resources to implement it. To date the AKTN has endorsed 4 multicentre RCTs, completed 3 RCTs and is currently coordinating 5 other research projects (4 RCTs and 1 observational study). The impact of this research is not only patient-centred but also has the capacity for significant cost-saving for the Australian healthcare system. Additional funding from the Australian Government has been secured and the AKTN is currently developing research projects across all patient populations that will be rolled out over the next 5 years.

The Australasian Sleep Trials Network

www.sleeptrials.net

Years	Members	Studies	Funding	Publications
10	Australia wide New Zealand	3 completed 7 current	$1-2.5m	10+

The Australian Sleep Trials Network (ASTN) is an inclusive consortium that was founded in 2005 to develop infrastructure to support Australasian multicentre trials in the field of sleep research. The network was formed to enable, facilitate and conduct large-scale multicentre investigator driven clinical trials of national and international significance, funded by Government or industry, that have potential to have a major impact on sleep health in the Australasian region.

The scope of research conducted by the network covers full range of sleep disorders, including insomnia, circadian disturbances, sleep breathing problems and neurological disorders. It is working currently on establishing Open Forums where researchers can discuss and develop sleep research projects, obtain help with funding approaches, and receive credentialing and common infrastructure support, particularly in statistics, trial design, health economics, outcome standardisation and recruitment. The ASTN provides researchers with expertise and resources for conducting of multicentre clinical trials in sleep health linking research projects to expertise in the banking of biological samples, genomics, data management and assessment of treatment outcomes for sleep disorders.

It represents Australia's clinical research capacity on a cross pharma investigator databank, the initiative driven by Janssen, Merck, and Lilly together with DrugDev.org to reduce redundant training and administration in the clinical trials process by allowing participating companies to mutually reference each other's' training and site inventory records.

Major Achievements

The ASTN is a participant in a recently sponsored Australian Government initiative to form the Cooperative Research Centre (CRC) for Alertness, Safety and Productivity, which provides leveraged funding to build critical mass in research ventures between end users and researchers. The objective of the program is to deliver significant economic, environmental and social benefits to Australia by supporting end user driven research partnerships to address clearly articulated major challenges. This program supports the development of strong links between academic researchers and innovative industry partners and facilitates long term collaboration, where the ASTN provides portal access for this consortium to the sleep researchers around Australia and New Zealand positioning the ASTN as an important gatekeeper for data standardisation and biobanking initiatives going forward and crucial for the ongoing sustainability of the network. The CRC will also act as an agent for the ASTN in relation to other large-scale trials and development work that might fall outside the scope of the newly funded CRC. In addition, a key component of CRC activity is a comprehensive education and training program that will involve significant levels of industry collaboration and engagement.

The Spinal Cord Injury Network

www.spinalnetwork.org.au

Years	Members	Studies	Funding	Publications
7	Australia Wide New Zealand	2 current	$450,000	N/A

The Spinal Cord Injury Network (SCIN) is dedicated to improving outcomes for patients with spinal cord injuries with a clear vision to facilitate recovery. This organisation, established as a company limited by guarantee in April 2008, has Deductible Gift Recipient status and is governed by a Board. Groups working in research development, clinical trials and evidence-based practice underpin the network's activities. SCIN works in partnership with other organisations and networks to ensure early adoption of best practice protocols for rehabilitation, acute care and ongoing health promotion.

A Code of Conduct has been drawn up to underpin the Spinal Cord Injury Network's vision of working together to facilitate recovery from spinal cord injury. The mission of the network is to unite the spinal cord injury community to optimise the quality of life and maximise recovery for the injury sufferers. SCIN facilitated the establishment and currently oversees the maintenance of the SpinalCARE Registry containing information about how many trials have being conducted, provides travel grants to spinal cord injury researchers in memory of Rosalind Nicholson, funds PhD students' research in the field and works to secure future funding for PhD scholarships.

Major Achievements

Close collaboration between the network and the National Trauma Research Institutes allowed for development of a strategic road map for the future research. Furthermore, the joint activity of the network and the Monash School of Public Health and Preventive Medicine led to development of the scoping document for a national spinal cord injury registry. The network has a strong focus on consumer engagement and multidisciplinary research.

The Australian Type 1 Diabetes Clinical Research Network

www.t1dcrn.org.au

Years	Members	Studies	Funding	Publications
5	Australia wide International	17 current	$25-50m	N/A

The principal goal of the Australian Type 1 Diabetes Clinical Research Network (T1DCRN) is to positively impact lives of people with type 1 diabetes in Australia through the support and promotion of clinical research. The launch of this organisation in 2010 has been made possible through a $5 million grant from the Australian Government and the Department of Health and Ageing (DoHA). The network brings together world-class researchers from multiple research fields to answer the most critical type 1 diabetes research questions to enable the efficient and effective delivery and adoption of clinical research, and build long-term research capacity in Australia.

The network's success in accelerating clinical research prompted over 250 young people to meet with 135 politicians from electorates across the country and speak about the realities of life with Type 1 Diabetes and the need for more research. In 2014 their effort culminated in a $35 million funding commitment from the Australian Research Council in the form of a Special research initiative, which is the largest ever single commitment to Type 1 Diabetes in Australia, and the network strives to deliver its promise to promote and accelerate diabetes-related clinical research.

The vision of the network is to accelerate the progress of Type 1 diabetes clinical research, resulting in real-life benefits and access to new treatments and therapies for people living with Type 1 Diabetes. In order to achieve this vision, the network aims to increase world-class clinical research, forge national and global partnerships for development of expertise and sharing resources in type 1 diabetes research. The network's effort in providing knowledge, data and sample sharing combined with its unique network building initiatives and policies, brings together the researchers, institutions, patients, industry and international networks to focus on patient benefit. It currently comprises 45 researchers across all states and territories in Australia. The network's governance arrangements cross disciplinary, geographical and institutional boundaries in order to achieve its global vision.

Major Achievements

Due to an ongoing support from the Juvenile Diabetes Research Foundation, the T1DCRN has retained and extended government confidence and support in the form of a new Special Research Initiative for $35 million from the Australian Research Council (ARC) to be invested from 2014 – 2018. This initiative will expand on previous initiatives and further develop the national collaborative network of researchers, creating a more connected and cohesive clinical research system. The network currently successfully coordinates 17 studies, four of which are late phase clinical trials. The IND trial investigating the role of Oral Insulin in Prevention of Diabetes in Relatives at Risk for Type 1 Diabetes Mellitus is managed in conjunction with a number of international organisations such as National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Allergy and Infectious Diseases (NIAID), National Centre for Research Resources (NCRR) and American Diabetes Association. A randomised, double-blind, placebo-controlled trial investigating effects of Intranasal Insulin in Children and Young Adults at Risk of Type 1 Diabetes (UNITII) received more than $16M of grant funding from NHMRC and Juvenile Diabetes Research Foundation.

The Interdisciplinary Maternal Perinatal Australasian Collaborative Trials Network

www.psanz.com.au/special-interest/impact

Years	Members	Studies	Funding	Publications
20	Australia wide New Zealand International	147 completed 150 current	$10-25m	146

The Interdisciplinary Maternal and Perinatal Australasian Collaborative Trials Network (IMPACT) was formed in 1994 as part of the then Australian Perinatal Society and, in 1997, it became a subcommittee of the Perinatal Society of Australia and New Zealand (PSANZ). The network is dedicated to improving outcomes for mothers and babies through the conduct of well-designed RCTs coupled with subsequent dissemination and application of trial results. The core values of IMPACT are collaboration, open communication, maintaining best practice to improve health outcomes, quality and relevance of the research, raising awareness of trials, investment in the future, trust and confidentiality, and partnership with mothers and their families.

Its significant expertise across Australia and New Zealand combined with grant-funded infrastructure has led to the establishment of successful trial coordinating centres focused on optimal maternal and perinatal health. IMPACT has conducted multiple high quality, collaborative, investigator-driven RCTs, the results of which have been incorporated into clinical practice, supporting evidence-based decision-making by consumers, health practitioners, and policy makers. The network is highly regarded for its action-oriented engagement with community, consumers and parents, healthcare and academic organisations, care professionals and researchers.

Major Achievements

The network has analysed the impact of RCTs conducted over recent years. These trials achieved both improved outcomes and cost saving with a maximum potential cost savings of $258 million per year. These trials covered five perinatal-related interventions: whole-body hypothermia for reduction of the risk of death or major sensorineural disability in newborns with hypoxic-ischaemic encephalopathy (ICE trial), a preventive care program to enhance child development and care-giver mental health was (VIBeS Plus trial), assessment of the caseload midwifery care to reduce the proportion of births by caesarean section (COSMOS and MANGO trials), provision of the improved management of asthma during pregnancy using a fraction of exhaled nitric oxide algorithm (MAP trial) and delivery of the continuous positive airway pressure to reduce the rates of death or bronchopulmonary dysplasia (COIN trial).

Therapeutic and Vaccine Research Program, Kirby Institute

www.kirby.unsw.edu.au/research-programs/therapeutic-and-vaccine-research-program

Years	Members	Studies	Funding	Publications
25	Australia wide International	>30 completed 5 current	>200m	>200

The Therapeutic and Vaccine Research Program (TVRP) was established in 2002 following consolidation of previously arranged structures within what was then the National Centre in HIV Epidemiology and Clinical Research (NCHECR) and is now known as the Kirby Institute. Over the nearly three decades of operation the TVRP has become a recognised coordinating centre for national and international research responsible for a range of clinical trials designed to assess the effectiveness of new HIV therapies, new treatment strategies or candidate vaccines for treatment and prevention of HIV and other virus diseases.

The TVRP has led a large number of clinical trials supported by competitive applications (national and international) and commercially funded phase I through Iv clinical trials. The TVRP collaborates directly with nearly 100 clinical centres in 18 countries on six continents.

The group has developed expertise in overcoming the complexities of regulatory and operational issues in these diverse settings as well as securing institutional support for UNSW to be formally identified as the Sponsor for all TVRP research.

Major Achievements

The TVRP has played a leading role in multiple high impact clinical trials that have provided definitive advice to clinicians and policymakers on the optimal management of patients with HIV. Work conducted by the TVRP has contributed substantially to the improved outlook for patients with HIV infection, both in developed as well as developing countries. It has played a role in undertaking a number of first in human trials of candidate therapeutic and preventive vaccine candidates for HIV infection based on recombinant gene technology and genetically modified organisms.

The TVRP also provides research leadership through the Program's role as an International Co-ordinating Centre for the INSIGHT network, a major international collaboration funded by the US National Institutes of Health through the National Institute for Allergy and Infectious Diseases for the conduct of large clinical trials that address strategic issues in HIV disease.

Trans Tasman Radiation Oncology Group

www.trog.com.au

Years	Members	Studies	Funding	Publications
26	Australia wide New Zealand International	32 completed 43 current	$25-50m	107

The Trans Tasman Radiation Oncology Group (TROG) is a global leader in radiotherapy research conducting high quality controlled clinical trials focused on investigation of the effects of radiation therapy to improve outcomes and quality of life for people affected by cancer. TROG was established in 1989 by the then seven radiotherapy centres across Australia and New Zealand and has over 1000 members. Its objective is to advance the study of cancers treatable with radiotherapy (breast, lung, prostate, skin, head and neck) and to contribute to a process of continual improvement in cancer treatment for the benefit of patients in the Trans-Tasman region and internationally.

TROG has a Central Operations Office that provides full trial management from the time of initial trial concept proposal through to completion and publication in medical journals.

TROG works with radiation therapy treatment centres and researchers to ensure that recruitment and data collection targets are being met, patient safety is monitored, data is being collated and primary/final endpoints are reported. TROG contributes to the generation of international standards, develops quality assurance procedures for credentialing, and incorporates the use of technologically advanced dosimetric phantoms and software to guarantee that researchers have access to the best available resources.

Major Achievements

TROG led the largest ANZ trial of 800 men with inoperable prostate cancer, (TROG 96.01) which demonstrated that radiotherapy preceded by hormone treatment reduces both local and metastatic recurrence of prostate cancer by approximately 60%.

The TROG 96.06 skin cancer trial conducted over 11 years and involving 200 patients from 7 cancer centres in Australia and New Zealand demonstrated that application of radiotherapy after a standard surgical procedure reduces chances of skin cancer recurrence by approximately 30%.

The TROG 89.04 oesophagus cancer trial showed that compared to standard treatment of either surgery or radiotherapy alone, concurrent radiotherapy and chemotherapy could improve 5-year survival outlook substantially.

Australian Government

Australian Clinical Trials

SEARCH FOR A CLINICAL TRIAL

www.australianclinicaltrials.gov.au

Information and resources for consumers,
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