The Clinical Oncological Society of Australia (COSA) is Australia’s peak multidisciplinary society for health professionals working in cancer research, treatment, rehabilitation and palliative care with over 1600 members. COSA is an advocacy organisation whose views are valued in all aspects of cancer care. COSA provides high-level clinical advice to Cancer Council Australia.
Key Recommendations

There is a distinct need for strategic planning within Australia’s cancer research community if Australian cancer research is to have an impact on the health of all Australians. The Clinical Oncological Society of Australia (COSA) recommends that a significant proportion of a national cancer research plan focus on support for clinical cancer research as:

- Clinical research is outcome and patient focussed.
- Clinical trials are a research tool that is applicable to all cancers.
- Clinical research encompasses the cancer spectrum from prevention to palliative care and includes observational, interventional and behavioural studies.

The pool of funding for clinical research in Australia has dramatically decreased over the last five years. COSA recommends that support for investigator-initiated cancer clinical trials be a priority for a national plan for cancer research, including:

- A considerable and strategic investment in clinical cancer research to ensure the effective and efficient improvement in health outcomes based on the best available evidence for cancer care and service provision.
- Increase in funding for research clinicians working in acute and community health services to ensure the translation of research outcomes into practice.
- Investment in the infrastructure required for clinical cancer research in Australia, including databases, biobanks, registries and support staff.

Formulation of a national cancer research plan presents the Cancer Research Leadership Forum (CRLF) with a unique opportunity to take the lead in supporting clinical cancer research in Australia. COSA has a strong record of advocating for clinical cancer research and looks forward to further opportunities to work with the CRLF to place clinical cancer research on the research funding agenda.
**Introduction**

There is a distinct need for strategic planning within Australia’s cancer research community if Australian cancer research is to have an impact on the health of all Australians. COSA commends the Cancer Research Leadership Forum (CRLF) for initiating the process of developing a national cancer research plan for Australia.

COSA has a history of initiatives in cancer research, specifically in relation to support for clinical research, with a focus on clinical trials. COSA has had particular success in bringing together stakeholders from clinical and research settings to discuss the challenges facing cancer research in Australia. COSA is a leader in devising strategies to overcome issues in a collaborative manner. These initiatives often take the form of a workshop, followed by a report that informs further discussion and used as an advocacy tool. These reports can be found on the COSA website (www.cosa.org.au) and include:

- Identifying our opportunities in translational research (2010)
- Models to improve efficiencies in Cancer Cooperative Trials Group activities (2010)
- Developing a nationally coordinated approach to biobanking for cancer clinical trials in Australia (2009)
- Tissue banking for cancer clinical trials (2008)
- Co-operative Clinical Trials in Cancer – the need for increased capacity (2002)

COSA supports the view expressed by the CRLF in the white paper that Australia needs greater investment in research into population health, health services, translation of basic research, psychosocial and survivorship issues as well as research focused on clinical questions. COSA is particularly concerned about the lack of support for clinical trials in Australia and the impact this will have on improving health outcomes for all Australians.

**Towards a national cancer research plan**

A plan of this scope has many purposes and audiences. COSA considers the following questions essential to the relevance and success of the plan:

- What is the primary purpose of the plan? Will it inform decision making by organisations that fund cancer research in Australia?
- Will lobby groups use the plan to advocate for a particular cancer research strategy to government?
- Is the plan accessible to consumers? How will consumers benefit from the plan?
- Is there a process for implementation of the plan? Who is responsible for this?
- What evaluation strategy is in place to measure the success of the plan?
- To reflect changes in the cancer research sector, when will revision of the plan occur?

Currently Australia does not have an umbrella body similar to the National Cancer Research Institute in the UK that represents the collective view of cancer research organisations. This means the success of a national cancer research plan in Australia will be restricted to organisations that choose to adopt its strategies and limited by the ability of lobbyists to convince governments to take up the plan at a national level.
The success of Cancer Australia’s Priority-driven Collaborative Cancer Research Scheme demonstrates the willingness of government to drive priorities in cancer research and of cancer research funding organisations to become partners with government. Perhaps the next challenge is integration of priority-driven cancer research into Australia’s clinics and hospitals as well as the biotechnology and pharmaceutical industries.

COSA, in partnership with Cancer Council Australia has developed clinical guidelines through use of a wiki platform to allow contribution from multiple parties located all over Australia. This type of approach is ideal for the collaboration and referencing required for formulation of a national cancer research plan. A centralised resource to allow cancer researchers to discuss the challenges they face and devise strategies to overcome them would also be a useful tool in the long term.

COSA recently made a submission to the Strategic Review of Health and Medical Research in Australia (McKeon Review) which highlighted the importance of clinical research for the well-being of Australians. Please see Attachment 1 for the complete submission from COSA to the McKeon Review. We expand on the themes of this submission below, with particular emphasis on clinical research as a cornerstone of any cancer research plan.

**Clinical cancer research directly improves patient outcomes**

Decades of research have documented the success of cancer clinical trials in improving long-term patient outcomes. The benefits of clinical research are clear:

- Clinical research reduces the burden of disease by improving treatments, enhancing care and developing ways to increase quality of life for patients and survivors.
- Clinical research finds ways to improve currently accepted standards of care, enhance patient safety, increase productivity, reduce cost and foster innovation.
- Clinical research facilitates the practice of evidence-based health care and benefits the health outcomes of all Australians, while also contributing to the development of the Australian health workforce and growth of the Australian economy.

Cancer research encompasses a broad range of studies from early drug development to the study of disease in animal models. The results of research projects often take more than 10 to 15 years to change clinical practice. In contrast, the involvement of clinicians in clinical trials allows the rapid translation of clinical trial results to the clinic, in some cases even before the trial has begun.

The benefit of conducting clinical trials in Australia is clear if we account for the time taken to implement clinical trial results from overseas. Figure one illustrates a hypothetical scenario demonstrating the timing of the outcomes of a trial performed in Australia, compared to another country (in this example the USA).
Clinicians in Australia become aware of the results of clinical trials performed overseas when a research conference publishes an abstract as part of the program. Complete results of the trial are available once an international scientific journal publishes the research. A systematic review by the Cochrane Collaboration found that the time from the date a clinical trial starts to the date of publication in a journal ranged from four to eight years. Following publication of trial results, clinical guidelines may incorporate this new evidence and ultimately changes to practice will occur. This process may lead to implementation of change in Australia many years after the clinical question was defined (Figure 1 panel A).

In contrast, the performance of clinical trials in Australia may see the translation of results into practice earlier, in some cases immediately following design of the study (Figure 1 panel B). This is a direct result of clinicians participating in clinical trials in Australia as they have early access to the improved standard protocols developed for clinical trials and evidence for improved interventions well before the trial results are published.

Clinical trials invariably compare interventions (a drug, device or protocol) currently used in the clinic with new interventions aimed at improving patient outcome. This inherently involves determining the optimal standard of care currently used around the world, before making any comparisons to new methods. Clinicians must establish the evidence base supporting the current standard of care by methodical review of the medical and scientific literature. This improves their understanding of the evidence for good practice, resulting in higher standards and improvements in the quality of care.

As clinicians realise the benefits of the new standard of care they start to incorporate these changes in the clinic immediately. This benefits many more patients than the number of participants in a
clinical trial, as clinicians implement the improved protocols regardless of whether or not patients are involved in the specific trial. Greater compliance and reduced variation in care protocols also occurs between sites participating in clinical trials. In fact, the effect of standardised, audited trial protocols on patient outcomes may be independent of the benefits of the intervention tested in the trial as demonstrated in the following case study.

**Case Study**

**TROG 02.02 improves radiotherapy protocol compliance and patient outcomes.**

A recent clinical trial designed by the Trans-Tasman Radiation Oncology Group to compare two treatment regimens for advanced head and neck cancer (TROG 02.02) gave the group some surprising results. The design of the trial required rigorous standardisation of protocols as it involved 89 sites in 16 countries. A quality assurance review of the radiation delivery protocol at each site participating in the trial formed part of this process.

All radiotherapy plans and radiotherapy documentation underwent review for compliance with the trial protocol. Radiation oncologists received feedback on compliance to treatment protocol and could amend the radiotherapy accordingly. Despite this, the trial demonstrated a 20% decrease in the overall survival of patients 2 years after receiving treatment at sites where radiotherapy protocols were not compliant with the trial.

While the trial found no benefit to patients for the chemotherapy drug tested, the group has seen the radiotherapy protocol from the trial implemented around the world due to the unexpected results from the quality assurance review.

**Clinical cancer research is relevant to all types of cancer**

Clinical cancer research can be coordinated and integrated across cancer types, including all those represented by members of the CRLF. Furthermore, performance of clinical research occurs across the entire spectrum of the disease, from prevention, diagnosis and treatment to palliative care.

Australia has 14 national Cancer Cooperative Trial Groups (CCTGs), with a record of investigator-driven research of an international standard (Appendix 1). These groups coordinate the majority of cancer clinical trials in Australia and encompass numerous disease sites, a range of age groups from paediatric to geriatric, specialists from different disciplines (most often acting in a voluntary capacity), consumers, data managers and biostatisticians, supported by a diverse group of administrators.

In 2005, COSA and the CCTGs received an NHMRC Enabling Grant of $1.84 million over five years. This funding promoted harmonisation and efficiency in cancer clinical trials in Australia by streamlining processes and procedures to ensure the optimal use of available resources, including the development of tools for protocol development, governance and enhancement of existing electronic data capture systems. This project is an example of the successful coordination of cancer research by engaging and resourcing groups with similar interests and needs.

The alliance between COSA and the CCTGs has highlighted the benefits of large-scale clinical research groups working together to achieve greater efficiency in processes and stakeholder engagement. In addition, the following statistics demonstrate the support for clinical trials within Australia:
• More than 18,000 Australians participated in clinical trials in 2009.\(^6\)
• In NSW, 70% of new enrolments to cancer clinical trials between 2004 and 2006 were to non-industry trials, initiated by single investigators or led by one of the CCTGs.\(^7\)
• Over six thousand clinical trials registered with the Australian New Zealand Clinical Trials Registry since its inception in 2005.\(^8\)

The need for funding clinical cancer research in Australia

The public perception that the pharmaceutical industry funds the majority of clinical trials is unfounded. Only 18.5% of the 6,436 clinical trials registered on the Australian New Zealand Clinical Trials Registry since 2005 have listed the commercial sector/industry as a funding source. The funds for the remaining trials come from government (23.4%), hospitals (11.8%), universities (13.4%), charities/societies/foundations (14.8%), and other collaborative groups (2.6%) or are self-funded/unfunded (12.3%).\(^9\) This variety of funding must continue if clinical cancer research in Australia is to remain sustainable and competitive.

The pool of funding for clinical research in Australia has dramatically decreased over the last five years. Funding schemes discontinued in recent years that supported clinical research include:

• Enabling Grants (National Health and Medical Research Council)
• NSW Cancer Trials Nurse and Data Manager Grants (this program was previously funded jointly by Cancer Council NSW and Cancer Institute NSW; however Cancer Council withdrew their funding in December 2011)
• Clinical Trials Network Support Grants (Cancer Institute NSW)

Clinical research in Australia currently competes for funding with every other health and medical research sector through the peer review systems of government agencies and not-for-profit organisations. While we support the independent review and accountability measures developed by these institutions, clinical research is inherently different to basic research. Clinical research and clinical trials in particular, may take much longer to complete, have fewer immediate measurable outputs, higher costs and greater regulation than non-clinical research. To account for these differences funding agencies should consider the evaluation of clinical research projects using a more relevant range of criteria.

The bias in the current peer review system towards basic research is clear when we consider the number of applications and success rate for clinical medicine, health services and public health research (Table 1). The NHMRC awards fewer grants to clinical research compared to basic research, despite the evidence that clinical research results in improved clinical outcomes. In addition, only a small proportion of the clinical research projects that receive NHMRC funding are for clinical trials. The reduced support for clinical research in the current system is not in alignment with demands made by the community for the rapid translation of research into improved clinical outcomes.\(^10\)
Table 1 NHMRC Project Grants success rate by Broad Research Area, 2011

<table>
<thead>
<tr>
<th>Broad Research Area (BRA)</th>
<th>Total Number of Applications</th>
<th>Number of Applications Funded</th>
<th>Proportion funded by BRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic Science</td>
<td>1721</td>
<td>437</td>
<td>25.4%</td>
</tr>
<tr>
<td>Clinical Medicine and Science</td>
<td>1173</td>
<td>232</td>
<td>19.8%</td>
</tr>
<tr>
<td>Health Services</td>
<td>132</td>
<td>22</td>
<td>16.7%</td>
</tr>
<tr>
<td>Public Health</td>
<td>343</td>
<td>80</td>
<td>23.3%</td>
</tr>
<tr>
<td>2011 Total</td>
<td>3369</td>
<td>771</td>
<td>22.9%</td>
</tr>
</tbody>
</table>

To optimise patient outcomes and health system effectiveness in Australia, it is essential to maintain an independent clinical research capacity through investigator-driven clinical trials, many of which the CCTGs coordinate. Commercially driven research may not focus on key clinical questions, particularly the role of non-drug interventions such as surgery and radiotherapy, optimal clinical practice protocols and psychosocial, supportive and palliative care. This also includes research into the comparative effectiveness of approved products, services and technologies, and pragmatic clinical trials to help with clinical decision-making.

COSA recommends that Australia make a considerable and strategic investment in clinical cancer research. This will result in the effective and efficient improvement in health outcomes based on the best available evidence for cancer care and service provision.

**Supporting the clinical cancer research workforce**

The performance of internationally competitive cancer research in Australia retains clinicians and scientists within Australian research institutes. Retention of this highly skilled workforce enables Australia to continue to build a reputation of innovation and excellence in cancer research that in turn attracts clinicians, scientists and funding from overseas. This pool of research expertise within Australia is then available to mentor and foster young researchers.

Participation of Australian health care providers in clinical research establishes local expertise in evidence based practice as well as promoting the understanding of the benefits and risks associated with change. Support for clinical research in Australia leads to improved training opportunities for clinician researchers and delivery of quality clinical education of an international standard. Moreover, support for clinical trials develops a culture of clinical investigation in the next generation of clinicians, ensuring the continuous use of previously generated evidence as the basis for new knowledge and hence improved health outcomes.

The delivery of quality research education and training in medical and health science faculties of Australian universities will help reduce the current gap between research and clinical practice. Embedding clinicians in laboratories and researchers in clinics will enable the transfer of knowledge and understanding between disciplines and enable better planning when establishing research projects.
COSA recommends that a national cancer research plan include priority funding for research clinicians working in acute and community health services to ensure the translation of research outcomes into practice.

**Providing infrastructure for clinical cancer research**

Provision of research infrastructure for cancer research encompasses:

- database design and support
- establishment and maintenance of biobanks
- coordinated, efficient multi-site ethics approval process
- establishment and support for research participant registries

There are currently two census points where cancer data collection is mandatory in Australia, at diagnosis (incidence) and at death (mortality). This means data regarding treatment outcome, quality of life and survivorship issues are seldom collected outside the context of a clinical trial. Electronic health systems offer enormous potential to streamline data management for cancer research, to enhance patient recruitment and enable the long-term tracking of research participants.

The establishment of independent tumour biobanks in Australia reflects their important role in supporting cancer research in Australia. Seven of these biobanks work cooperatively through the Australasian Biospecimen Network. The recently ceased NHMRC Enabling grant scheme funded some of these biobanks and they are struggling to find replacement funds. Biobanks are a vital resource for cancer research now and in the future and must be a key component of a national strategy for cancer research in Australia. Importantly, the funding of biobanks in the context of clinical trials allows the connection between tissue for future studies and clinical outcomes unknown at the time of collection.

The majority of cancer clinical trials in Australia involve a number of sites in order to facilitate the recruitment of the required number of participants. Each site must obtain ethical and governance approval to participate in the project. The NHMRC established the Harmonisation of Multi-centre Ethical Review (HoMER) program to streamline this process. Despite its introduction around Australia, a number of factors continue to hamper the implementation of this system, frustrating researchers and impeding cancer research in Australia.

Public surveys show widespread support for the concept of clinical trials as an important means of developing superior medical care. However, only a small proportion (2% to 3%) of eligible patients enrol in cancer clinical trials. At present, there is no centralised, automated system for patients to register their interest in participating in clinical trials in Australia. Army of Women in the US and Register4 in Australia are pioneering the way by developing online communities of women interested in participating in breast cancer research projects. The development of Australia’s electronic health system has enormous potential to increase participation in clinical trials and disease prevention programs by linking clinical trials recruiting participants to consumers interested in participating in research projects.

COSA recommends that Australia invest in the infrastructure required for clinical cancer research in Australia, including databases, biobanks, registries and support staff.
**Acknowledgements**

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**Contact Details**

For further information, please contact:

Marie Malica  
Executive Officer COSA  
Clinical Oncological Society of Australia (COSA)  
GPO Box 4708  
Sydney NSW 2001  
Ph: (02) 8063 4160  
Email: marie.malica@cancer.org.au
Appendix One – Cancer Cooperative Trial Groups in Australia

Cancer Cooperative Trials Groups (CCTGs)

Australia has 14 national cancer cooperative trials groups, with a record of world-class research. COSA and the Cancer Council have welcomed Commonwealth support for these groups through Cancer Australia and continue to advocate for increased and ongoing government funding for independent cancer clinical trials as we prepare for the increase in cancer incidence and prevalence.

Australasian Sarcoma Study Group (ASSG) aims to improve outcomes for sarcoma and related tumours in the Australian community by undertaking outstanding research.

Australasian Gastro Intestinal Trials Group (AGITG) is Australia’s largest independent non-profit organisation conducting clinical trials into gastrointestinal cancers.

Australasian Leukaemia & Lymphoma Group (ALLG) is the only not for profit organisation designing and delivering investigator initiated clinical trial research into blood cancers.

Australasian Lung Trials Group (ALTG) is a multi-disciplinary organisation dedicated to reducing the incidence, morbidity and mortality of lung and thoracic cancer in Australia and New Zealand.

Australian New Zealand Breast Cancer Trials Group (ANZBCTG) conducts an independent, collaborative breast cancer clinical trials research program to save lives from breast cancer.

Australian and New Zealand Children’s Haematology and Oncology Group (ANZCHOG) are the leading body representing the interests of children and adolescents with blood diseases and cancer.

Australia New Zealand Gynaecology Oncology Group (ANZGOG) supports collaborative research to improve outcomes of women with gynaecological malignancies through randomised clinical trials.

Australia New Zealand Melanoma Trials Group (ANZMTG) coordinates and conducts quality research for melanoma control.

Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP) develops and conducts cancer research in urogenital and prostate cancers.

Cooperative Trials Group for Neuro-Oncology (COGNO) aims to conduct investigator initiated and collaborative group trials addressing important clinical questions in patients with brain tumours.

Palliative Care Clinical Studies Collaborative (PaCCSC) is a national multicentre research network to support clinical studies in palliative care.

Primary Care Collaborative Cancer Clinical Trials Group (PC4) develops and conducts cancer research in primary care.

Psycho-oncology Cooperative Research Group (PoCoG) aims to develop capacity and collaboration to conduct large-scale, multi-centre psycho-oncology and supportive care research.

Trans-Tasman Radiation Oncology Group (TROG) is a cooperative multidisciplinary organisation dedicated to the control of cancer through quality multicentre research into radiotherapy.
References

2. Figure reproduced with permission from Professor John Zalcberg.