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DISCUSSION PAPER

Integrating Cardio-Oncology Across the Research Pipeline, Policy, and Practice in Australia—An Australian Cardiovascular Alliance Perspective

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Over 18 million people worldwide were diagnosed with cancer in 2020, including over 150,000 people in Australia. Although improved early detection and treatment have increased the survival rates, cardiotoxic treatment and inadequate management of cardiovascular risk factors have resulted in cardiovascular disease (CVD) being one of the leading causes of non-cancer-related death and disability among cancer survivors. International guidelines outline the standards of care for CVD risk surveillance and management. However, Australian cardio-oncology policies and clinical guidelines are limited. There is increasing growth of cardio-oncology research in Australia and support from leading Australian professional bodies and advocacy and research networks, including the Cardiac Society of Australia and New Zealand, the Clinical Oncology Society of Australia, the National Heart Foundation of Australia, and the Australian Cardiovascular Alliance (ACvA). Thus, opportunities to drive multidisciplinary cardio-oncology initiatives are growing, including grant funding, position statements, and novel research to inform new policies. The ACvA has a unique flagship structure that spans the translational research pipeline from drug discovery to implementation science. This article aims to highlight how multidisciplinary cardio-oncology innovations could intersect with the seven ACvA flagships, and to showcase Australian achievements in cardio-oncology thus far. We summarise eight key priority areas for future cardio-oncology research that emerged. These strategies will strengthen cardio-oncology research and care in Australia, and drive new guidelines, policies, and government initiatives to ensure equity in health outcomes for all cardio-oncology patients.

Keywords Cardio-oncology • Cardiology • Translational research • Public health

Introduction

Globally, over 18 million people were diagnosed with cancer in 2020 [1]. In Australia, over 151,000 people were diagnosed with cancer (excluding skin cancer) in 2021, which is estimated to rise by 22% by 2031 [2]. Improved early detection and treatment techniques have resulted in increased 5-year survival rates across cancer types [3]. However, cancer treatments, such as chemotherapy, radiation therapy, and molecular and immunotherapies, have significant cardiovascular (CV) effects by potentially damaging critical structures of the heart and blood vessels. Some toxicities are further potentiated when coupled with inadequately managed CV risk factors including hypertension, dyslipidaemia, smoking, physical inactivity, type 2 diabetes, and alcohol intake [4]. As a result, CV disease (CVD) has been found to be a leading cause of non-cancer-related deaths among patients with cancer globally including children [5], and accounts for over half of non-cancer-related deaths in Australians diagnosed with cancer [6].

Internationally, this clinical need has prompted the emergence of "cardio-oncology," a discipline aimed at improving CV health of people living with and beyond cancer. As this population of patients continues to grow, new challenges are emerging for policy makers, health providers, researchers, and patients, including the collection of high quality patient data, siloed clinical care, limited resources, and delivery of cardio-oncology education to health providers and patients [7]. There are further inequities in access, quality, and outcomes of care among underserved populations, including Aboriginal and Torres Strait Islander peoples, people with multimorbidity, and people living in regional, rural, and remote communities [8–14].

Cardiovascular and oncology experts across the world have mobilised to develop new cardio-oncology guidelines and recommendations for adult and paediatric populations [15–17], and quality indicators and priorities for improved cardio-oncology care [18–22]. In Australia, policies, clinical guidelines, and research about risks and management of cancer survivors' CV health are limited but rapidly evolving. For example, there are limited cardio-oncology guidelines for adults in Australia, but a nationwide survey of oncology, haematology, and cardiology specialists demonstrated high levels of support for developing Australian cardio-oncology guidelines and cardio-oncology services [23]. Moreover, Australian researchers have recently called for equitable solutions to cardio-oncology care [24] and strategies to facilitate care coordination [25]. Cancer Australia established "shared care" survivorship guidelines for joint delivery of follow-up care by oncologists and general practitioners [26] to overcome barriers of multidisciplinary care coordination for health care professionals.

To accelerate the expansion of the field of cardio-oncology within Australia, leading Australian professional bodies and advocacy and research networks, including the Cardiac Society of Australia and New Zealand (CSANZ), the Clinical Oncology Society of Australia (COSA), the National Heart Foundation of Australia (NHFA), and the Australian Cardiovascular Alliance (ACvA) have been driving cardio-oncology innovations and multidisciplinary solutions. These include grant funding, position statements, and novel research to inform new policies. For example, the NHFA established two cardio-oncology strategic grants (Australian dollar [AUD] $1 million, each), which were awarded to projects that (1) address cancer inequities and improve CV health for Aboriginal and Torres Strait Islander people with

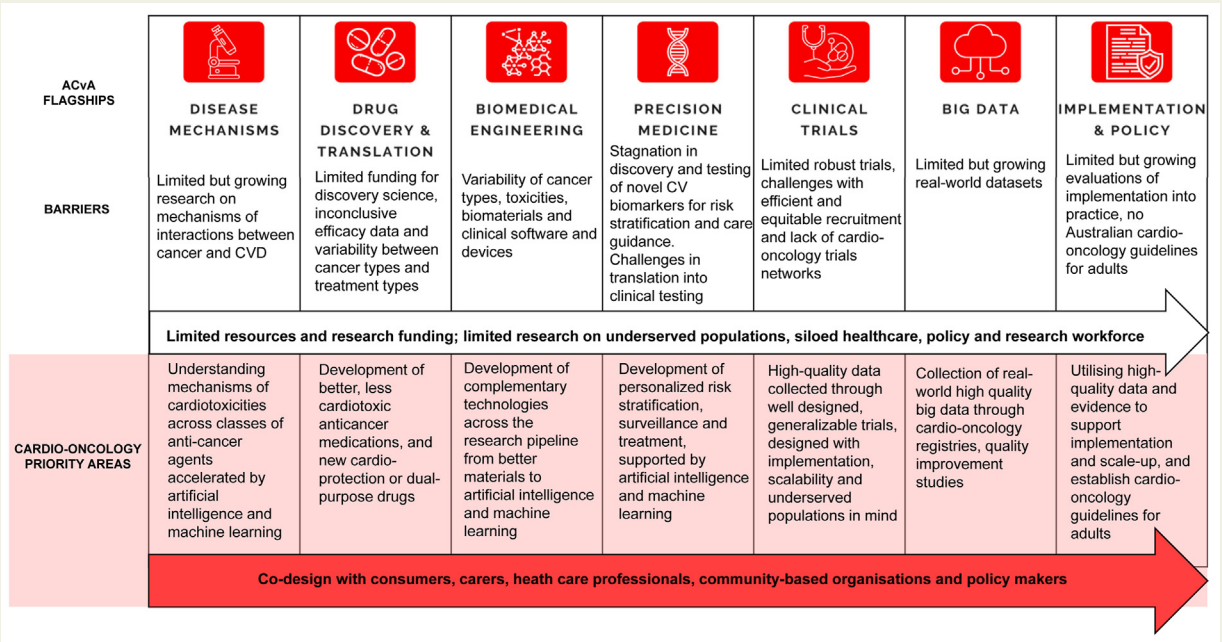

Figure Interrelationships between Australian Cardiovascular Alliance (ACvA) Flagships; barriers that each can help address; and, cardio-oncology priority areas.

cancer and (2) establish a national network of multidisciplinary cardio-oncology services [27]. Moreover, CSANZ and COSA established a joint multidisciplinary cardio-oncology working group that aims to improve CVD outcomes for people living with and beyond cancer in Australia by providing, developing, and facilitating discipline-specific education, training, and clinical standards of care, and to highlight key priority areas for improvement and ongoing development [20]. Coordination of innovations across the bidirectional research translation pipeline will be an important next step.

The ACvA is an Australian not-for-profit leadership body targeting the advancement of heart, stroke, and vascular disease research. The ACvA is a comprehensive collaboration of CV research bodies and scientific societies, individual researchers, industry, and non-government organisations in Australia. The ACvA is uniquely positioned to leverage key interactions between Australia's strong research capability and the health system to improve health outcomes and reduce costs. Advocacy by the ACvA has supported the introduction of the Australian Medical Research Future Fund–funded AUD $220-million Cardiovascular Health Mission [28], which has included strategic research funding in cardio-oncology. All initiatives have introduced strategies to enhance career opportunities and cultural shifts with mentorship and support for early and mid-career researchers. Moreover, ACvA has established seven pillars of research, called 'flagships', that span the translational pipeline from basic science to implementation and policy, and provide opportunities for cardio-oncology research in each (Figure). The flagship structure aims to promote collaboration and research excellence, and brings together the best teams to develop solutions for CVD that will positively affect the community. Spanning all flagships is the newly established ACvA Cardio-Oncology Working Group, which aims to enhance research collaborations, activities, and capacity building in cardio-oncology. This article aims to highlight how innovative and multidisciplinary cardio-oncology research initiatives could intersect with the seven ACvA flagships, and to showcase some of the achievements in the field of cardio-oncology within Australia thus far. We will also summarise priority areas for future multidisciplinary initiatives.

The Potential Intersection of Cardio-Oncology With the Seven ACvA Flagships

Disease Mechanisms

The cardiotoxicity of chemotherapy has been known since the 1960s. To improve risk stratification, early detection, and treatment of different forms of cardiotoxicity, we need to improve our understanding of the pathophysiology behind different types of cardiotoxicity and the interactions between different drug classes by fostering more interdisciplinary research between the fields of oncology and CVD. There is accumulating clinical and preclinical data that suggest an interdependence and biological overlap between cancer and CVD, based on commonality of pathophysiological mechanisms (e.g., inflammation, redox stress, abnormal

metabolism, and mitochondrial dysfunction). While the classic pathophysiology of anthracycline-induced cardiotoxicity has been well described, new research has continued to expand our understanding of its mechanisms. For example, it was previously thought that this cardiotoxicity was "irreversible." New research has shown that it may be reversible if detected and treated early, with a time-dependent reduction of treatment responsiveness [15]. Moreover, different Australian research groups have recently described associations between anthracycline cardiotoxicity and new mitochondrial pathways [29], and single nucleotide polymorphisms in a paediatric cohort [30]. Other Australian research groups have examined mechanisms underlying CV toxicities of several classes of anticancer drugs, such as Bruton tyrosine kinase inhibitors [31] and proteasome inhibitors [32]. Development or exacerbation of hypertension as an adverse effect of anticancer therapies is a good example of an emerging cardiotoxicity of several established and new anticancer drug classes [15]: more than 11 classes of anticancer drugs have been linked to the development of hypertension, involving at least five different major physiological processes via dozens of signalling cascades [33]. Even in the paediatric population, there is an up to 27% incidence of hypertension (data courtesy of the Australian Cardio-Oncology Registry [ACOR]). However, the precise mechanisms of cardiotoxicity of most anticancer agents are poorly understood, hampering our efforts to develop better ways of early detection and targeted treatments or preventative strategies. Collaboration across research groups, institutions, and flagships (including the *Biomedical Engineering* flagship) is likely the best strategy to efficiently advance our understanding of the complex interactions between dozens of anticancer drug classes (spanning thousands of drugs) and CV health. For example, artificial intelligence (AI) approaches including machine learning can help advance our understanding of disease mechanisms by allowing assessments of several biological parameters and large-scale transcriptomic and genomic data sets to help identify new cardiotoxic pathways and guide precision cardio-oncology.

Drug Discovery

A recent Australian study found that 55% (108,175 of 198,325) of people dispensed a cancer medicine between 2005 and 2021 were dispensed at least one potentially cardiotoxic medicine, and the number of people exposed to potentially cardiotoxic medicines more than quadrupled during the study period [34]. There are currently limited cardioprotective agents in routine clinical use in adult oncology, which is in part due to disparity in investment in fundamental drug discovery science between the fields of cancer and CVD. Recent investments in cancer research have led to a surge in the development of effective anticancer treatments, accounting for 40% of the global clinical pipeline, with over 1,600 products tested and launched in the last 5 years [35]. Comparatively, only 8% of drugs in development are for CVD indications [36]. Some CV drugs, such as beta-blockers and statins, have been investigated for the dual mechanism of cardioprotection and as an anticancer therapy [37–40]; however, the results are inconclusive and vary by cancer type and drug specificity. For example, evidence from a recent meta-analysis of epidemiological and perioperative studies [38], and an Australian population-based cohort study of 3,844 women with CV conditions who underwent surgery for ovarian cancer [39], found that beta-blockers conferred a survival benefit. However, the same meta-analyses found reduced survival for patients with endometrial, head and neck, or prostate cancer. Thus, caution has been advised for the interpretation of these observational effectiveness data [41]. Indeed, even recent trials of statins have shown discrepant results, and while weak results in favour of cardioprotective therapies have been observed in meta-analyses, the benefit would not always justify the risk of developing side effects [42,43]. However, the mechanistic overlap between pathogenesis of cancer and CVD begs the question of whether there can be a cardioprotection "holy grail," that is, a drug that has both anticancer and cardioprotective properties. Work from an Australian research group has been recognised with an ACvA Award for the identification of the drug (bisantrene), which has a dual role as an anticancer and cardioprotective agent [44]. Therefore, drug discovery/repurposing may be a promising research focus in the ACvA *Drug Discovery* flagship through development of more personalised and equitable cardioprotective therapies.

Biomedical Engineering

Biomedical engineering offers a diversity of solutions for cardio-oncology. Tools, software, and applications for better imaging, physiological and remote assessment, and monitoring of patients in both hospital and ambulatory settings would be invaluable. Development of simple eHealth or mHealth solutions and apps can be used by patients and health care professionals to improve early detection, monitoring, and patient-reported outcomes (PROMs) and patient-reported experience measures (PREMs) (e.g., satisfaction with clinical care) [45–48]. Australian researchers have found low-cost, scalable lifestyle-focussed text message programs effective for improving CV risk factors such as physical inactivity, high low-density lipoprotein cholesterol or blood pressure, and unhealthy diet for patients with CVD [46,49]. This work is now being assessed for effectiveness for breast cancer survivors in a multicentre effectiveness-implementation randomised controlled trial (RCT) in primary care, including remote collection of PROMs and PREMs (funded by the National Health and Medical Research Council of Australia [Grant Identfication 2017575] and the World Cancer Research Fund International). Wearable technologies are also being assessed within ACOR paediatric studies for improving cardiac surveillance in the ambulatory setting ("Beat 2 Beat"; NCT05615376). However, there has been considerable interest in the development of more advanced technologies. Artificial intelligence (AI)

applications can help guide health care professionals to better and earlier prognostication and diagnosis of CV complications across cancer types and therapies [50]. Additionally, biomedical innovations specific to each subtype of cardiotoxicity need to be developed in parallel. For example, improved stent technology, including biomaterial stent systems, can act as a carrier for cell and growth factor delivery for CVD, which can be accelerated by specific anticancer drugs, including immune checkpoint inhibitors [13,15].

Precision Medicine

Development of personalised medicine tools can help patients and health care professionals to appropriately manage patients' cardiotoxicities, health promotion, and preventative care from the time of diagnosis. Personalised medicine could integrate novel drug discoveries from the *Drug Discovery* and *Disease Management* flagships, and identify novel imaging, blood, molecular, and clinical biomarkers to improve risk stratification. At present, the field of cardio-oncology largely relies on less personalised use of conventional CV biomarkers for risk stratification, such as troponins and N-terminal prohormone of brain natriuretic peptide [51], and conventional CV imaging [52]. However, newer echocardiographic techniques, such as global longitudinal strain, have emerged as more sensitive strategies [51,52], as they provide better and earlier predictive value [15]. Substantial advances have also been made in clinical parameter-based risk stratification, with the development of the baseline risk stratification proformas for the typically used anticancer drugs through evidence and expert opinion [53]. Use of both strategies is now advocated in the international guidelines [15]. However, CVD risk factors may co-exist within an individual and may interact with each other and with the specific cancer treatment regimen [53], which needs to be further explored. The Newcastle Centre of Excellence in Cardio-Oncology is currently running a prospective longitudinal study (funded by two NHFA Future Leader Fellowships and a NSW Health CV Capacity Building Grant) investigating a combination of clinical, imaging, and established and novel blood biomarkers for risk stratification and early detection of cancer therapy–associated cardiotoxicity, with preliminary results probably available in 2024. In addition, collaboration with the *Biomedical Engineering* flagship could support the use of AI and machine learning techniques to analyse this wealth of biological, imaging, and clinical data to help guide more individualised approaches to cardio-oncological care. Importantly, the application of risk stratification proformas is intended to enhance personalised care and safeguard limited health care resources [53]. There is a need to investigate whether existing or new proformas can meet the needs of underserved populations such as Aboriginal and Torres Strait Islander peoples, who tend to be diagnosed with both cancer and CVD at a younger age than non-Indigenous Australians.

Clinical Trials

Robust clinical trials to guide clinical practice in cardio-oncology are increasing; however, they are still quite limited. This is evidenced by the latest international cardio-oncology guidelines [15], which include 272 recommendations, of which only seven have level A evidence (i.e., supported by multiple RCTs or a meta-analysis), 57 have level B evidence (i.e., derived from a single RCT or multiple non-randomised studies), and most (207 recommendations) have level C evidence (i.e., based on expert opinion) [17]. The many barriers, in addition to cardio-oncology being a relatively new field, include absence of well established cardio-oncology clinical trials networks, competing cancer therapy trials, and lack of equity in recruitment, all of which can lead to delayed recruitment targets and reduced external validity (i.e., generalisability) and achievement of clinically meaningful outcomes.

It is critical for cardio-oncology (and all) RCTs that inform care and health outcomes to be developed in ways that promote equity for all participants in order to improve the external validity of the results [54]. In Australia, Aboriginal and Torres Strait Islander people, people from culturally and linguistically diverse backgrounds, and people who live in regional and remote areas are under-represented in clinical trials [55,56]. The barriers to participation for patients include lack of awareness about trials, limited time and resources to attend trial visits, mistrust or fear of researchers and the medical system, and culturally inappropriate or unclear trial promotional materials [57]. In cardio-oncology trials, there are additional barriers for patients and health care professionals, including lack of awareness about cardiotoxicities, management of CV risk factors, and access to culturally appropriate resources [58,59]. For example, a recent audit of consumer-focussed information found that there was very little information dedicated to CV health after cancer offered by Australian health authorities. Furthermore, most available information was superficial in its coverage, required above average health literacy levels to read and understand, and did not contain actual advice to manage risk; in addition, none was deemed specific to, or inclusive of, Aboriginal and Torres Strait Islander peoples [59].

There are several strategies to improve trial participation that span the ACvA flagships. First, codesigning RCTs, trial materials, and cardio-oncology resources more generally with patients, health care professionals, policy makers, and other stakeholders is key [20] and could be supported by the *Implementation and Policy* flagship. Second, collaboration with the *Biomedical Engineering* flagship could involve the use of eHealth strategies, including websites, social media, and ePROs (electronic patient-reported outcomes), to educate patients and health care professionals, increase reach, awareness, and access to trials (especially for underserved populations), reduce recruitment delays, and facilitate remote follow-up data collection [60]. As a start, members of the ACvA Cardio-Oncology Working Group have codesigned and produced a series of e-learning modules for

health professionals to increase diversity, equity, and inclusion of Aboriginal and Torres Strait Islander people in clinical trials [61]. A collaboration with the *Big Data* flagship could involve incorporating national registries into trial designs to reduce time to identify and recruit eligible patients and/or facilitate collection of follow-up data [62]. In this context, the *Clinical Trials* flagship can also leverage its existing national network embedded in the health system, and international collaborations (such as the International Cardio-Oncology Society and other societies), to bring together, coordinate, and/or lead well-designed (inter)national cardio-oncology trials and produce high quality evidence for improving health outcomes for all. Several examples of recently completed and ongoing cardio-oncology trials in Australia are presented in Table [63–65], while more trials (including the SIT-STILL and CURATE-THERAPIES trials in paediatric populations, based on the motivational CanMOVE intervention [66]) are being planned in the near future.

Big Data

Conduct and analysis of multicentre international RCTs and their implementation into clinical practice and policy take several years; however, the guidance on management of cardio-oncology patients is needed now. In the meantime, big data, including observational and administrative data sets, have been used to inform many recommendations in the European Society of Cardiology cardio-oncology guidelines [15]. The *Big Data* flagship could use large-scale data linkage sets to provide timely insights into key concerns (including needs of underserved populations and gaps in cardio-oncology services), and through causal inference methodology, investigate the effects of anticancer therapies, cardioprotective drugs, and clinical care pathways among representative cancer cohorts. For example, a recently established dedicated online Global Cardio-Oncology Registry (G-COR) aims to provide the largest data set of its kind with over 120 sites in more than 21 countries, and to facilitate global cardio-oncology collaboration and innovations [67]. Australians, including members of the ACvA Cardio-Oncology Working Group, are involved in this initiative, including membership in the G-COR Scientific Executive Committee [67]. Furthermore, others are in the process of establishing a national data set from cardio-oncology clinics and assessing priorities for underserved populations. Two other examples are the SOLVE-CHD program, a 5-year initiative to digitise data from national cardiac rehabilitation and secondary prevention programs, and the National Echo Database Australia [68], which is the largest database of echocardiographic data with individual patient linkage to mortality through the National Death Index. While these two programs are not specifically set up for cardio-oncology patients, data could be used to identify important differences in clinical and patient-reported outcome measures, including mortality thresholds and cardiotoxicities. With several large data sets becoming available, collaboration with the *Precision Medicine* flagship offers immense opportunities for integration of AI and machine learning to develop various risk prediction, risk stratification, and surveillance tools that are cost-effective and can be trained for specific population groups to increase their sensitivity and specificity.

Implementation and Policy

The *Implementation and Policy* flagship could leverage engagement with government, industry, and research partners, and data from other flagships (such as *Drug Discovery*, *Clinical Trials*, and *Big Data*) to advocate for the development of a national best practice policy, and implementation into practice. For example, several dedicated cardio-oncology programs now exist across Australia, with data collection that spans the seven ACvA flagships. One example is the Newcastle Cardio-Oncology Program (established in 2017) in the Hunter New England Local Health District in New South Wales that incorporates fundamental discovery studies (preclinical in vitro and ex vivo and patient-derived human inducible pluripotent stem cell–derived cardiomyocytes), drug discovery and repurposing studies, translational and clinical research, and clinical service delivery for a comprehensive bench-to-bedside approach. Thus far, the program has been used by more than 550 patients attending over 2,200 visits, with over 20,000 patients in the database. Service delivery data from this cardio-oncology program resulted in direct positive effects on patients' cardiac health outcomes: of the first 250 patients referred to the program's dedicated cardio-oncology clinic, only 9% required interruption or change in cancer therapy due to a cardiac issue [69]. Patients found the program helpful for education, health management, and continuity of care, and felt more satisfied with their health care team and patient–clinician communication [70]. Results also revealed challenges in *accessing* cardio-oncology care, especially for patients living in regional, rural, and remote locations [71], which led to expansion of the service to three regional and rural sites (funded by a 2023 Cancer Institute NSW Accelerated Research Implementation Grant). Moreover, the fundamental science arm of the program has successfully engaged with industry partners aiming to deliver an anticancer drug with cardioprotective properties [72], leading to upcoming human trials [73]. In 2022, the Newcastle Cardio-Oncology Program became the first cardio-oncology program in Australia to receive the Top (Gold) Tier accreditation as a "Center of Excellence in Cardio-Oncology" from the International Cardio-Oncology Society in recognition of the program's excellence in clinical care, research, and education [74].

Another example is the ACOR and Biobank (established in 2018) [75]. ACOR is an integrated research program across 13 institutes nationally in both the paediatric and adult sector. ACOR collects data across 150 end points including demographics and traditional and novel therapies (e.g., molecular therapies, chemotherapy). Its research program includes assessing pharmacogenomic

Table **Examples of Australian cardio-oncology RCTs.**

Trial name, recruitment status	Population, setting	Intervention; comparator	Primary outcome	Results
SUCCOUR RCT, complete [63]	n=311; adult patients undergoing anthracycline-based chemotherapy with another risk factor for heart failure 28 sites (international)	LVEF and GLS surveillance via echocardiography with GLS-guided initiation of cardioprotection; vs usual care	Difference in LVEF from baseline to 1-yr follow-up	Not significant, but intervention participants who received cardioprotective therapy had significantly lower reduction in LVEF at 1-yr follow-up
BREXIT RCT, complete [64]	n=104; adult women with early-stage breast cancer undergoing anthracycline-based chemotherapy One site (hospital)	12-month physical activity program (3–4 days aerobic and resistance training); vs usual care (encouraged to be physically active, according to national guidelines)	Functional disability (VO_2 peak $\leq$18.0 mL·kg−1·min−1) at 12 mo	No difference in VO_2 peak at 12 mo, but among participants who adhered to the program, functional disability was prevented
SMART-BREAST RCT, complete [65]	n=103; adult women with early-stage breast cancer One site (hospital)	Smart phone–based physical activity intervention; vs usual care (encouraged to access physical activity resources)	Change in 6-minute walk test distance (m) at 12 mo	Significant difference between groups (median Δ46 m [IQR, 28–63] vs Δ8 m (IQR, –10 to 35; $p<0.001$)
SUCCOUR-MRI RCT, ongoing (ACTRN12620001094965)	n=1,100 (screening target); adult patients planned to undergo treatment of anthracycline-based chemotherapy with one of the following: trastuzumab treatment, or tyrosine kinase inhibitors, or anthracycline dose >450 mg/m^2, or prior treatment with anthracycline, or chest-directed radiotherapy for another cancer, or increased risk of heart failure	Patients with a reduced GLS but not LVEF randomised to cardioprotection (ramipril and metoprolol)	Change in cardiac magnetic resonance (CMR) ejection fraction from baseline to 1 year	Trial still ongoing
SOCRATES trial, ongoing (NCT05180942)	n=180; adult patients with melanoma treated with immune checkpoint inhibitors 12 sites (hospitals)	40-mg atorvastatin; vs usual care (no treatment)	Progression of atherosclerosis measured by computed tomography coronary angiography at 4 wks	Trial still ongoing

predisposition to anthracycline cardiotoxicity using patient-derived human-induced pluripotent stem cells as functional models [76]; investigating novel approaches to identifying poor cardiac reserve compared with standard of care [77]; and, establishing and reporting on the first cardio-oncology clinics in paediatrics following the ACOR-led paediatric cardio-oncology guidelines [16]. ACOR has established cardio-oncology clinics in Victoria (paediatric) and New South Wales (paediatric and adult). To date, ACOR includes data from 600 patients nationally. Patient data from ACOR can also be linked to the Australian Medicare Benefits Schedule and Pharmaceutical Benefits Scheme for tracking of health system use and therapy-related cardiac dysfunction, and assessment of the cost-effectiveness of cardio-oncology care.

Although cardio-oncology clinics seem promising, high quality assessments of different models of care will be critical. For example, ACvA members led an implementation quality improvement program called "QUEL" with linked data from 15,040 patients with CVD across 50 Australian primary care practices [78]. These data have since been used to assess the use of cardioprotective drugs, chronic disease management plans, and mental health care among cardio-oncology patients, which was found to be suboptimal [79]. Another Australian team is piloting a multidisciplinary approach to managing cardiac risk of patients with cancer by establishing referral pathways between radiation-oncology and cardiology [80]. A novel nurse-led cardio-oncology clinic was awarded the 2023 CSANZ Cardiovascular Nursing Clinical Innovation Award (2023 CSANZ Scientific Sessions), while pharmacist-led cardio-oncology clinics are being assessed in the paediatric setting (Children's Oncology Group Conference, Atlanta, 2023). It is only through converging multidisciplinary efforts and government support that implementation and policy change can be achieved.

Future Directions and Conclusions

With many emerging opportunities in cardio-oncology, a multidisciplinary, evidence-based, equity-driven, and accessible approach to cardio-oncology research and care that calls on the whole research pipeline is needed. The key priority areas and strategies that have emerged are listed in Box 1 and include the following: (1) improved understanding of mechanisms of cardiotoxicity; (2) development of better, less cardiotoxic anticancer drugs while advancing the field of cardioprotection or dual-purpose drugs; (3) development of complementary technologies across the entire research pipeline ranging from improved materials to AI support; (4) development of more personalised solutions for risk stratification, surveillance, and treatment, which should include novel AI and machine learning approaches to precision cardio-oncology; (5) supporting all these new strategies through well-designed and generalisable clinical trials; (6) collection of real-world big data through cardio-oncology registries and quality

Table. (continued).

Trial name, recruitment status	Population, setting	Intervention; comparator	Primary outcome	Results
COP-RCT, ongoing (ACTRN12621000928819)	n=70 adults who have recovered from cancer therapy–related cardiac dysfunction One site (hospital)	Supervised withdrawal of cardioprotective therapies; vs usual care (continuing cardioprotective therapies)	Difference in composite end point of relapse in cardiac dysfunction at 6 months, defined by: 1) reduction in 3D LVEF between 10% and 50%; 2) heart failure requiring hospital admission; or 3) worsening heart failure requiring medical treatment	Trial still ongoing

Abbreviations: RCT, randomised controlled trial; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; IQR, interquartile range; 3D, three-dimensional; SUCCOUR, Strain sUrveillance of Chemotherapy for improving Cardiovascular Outcomes; BREXIT, BReast cancer EXercise InTervention; SOCRATES, SOluble Cyclase stimulatoR in heArT failurE patientS; COP-RCT, Cessation Of Pharmacotherapy in Recovered Chemotherapy-induced cardioToxicity.

Box 1. Key priority areas for cardio-oncology research in Australia.

1	Improvement of our understanding of mechanisms of cardiotoxicity
2	Development of better, less cardiotoxic anticancer drugs while advancing the field of cardioprotection or dual-purpose drugs
3	Development of complementary technologies across the entire research pipeline ranging from improved materials to artificial intelligence support
4	Development of more personalised solutions for risk stratification, surveillance, and treatment, which should include novel artificial intelligence and machine learning approaches to precision cardio-oncology
5	Supporting new research strategies through well-designed and generalisable clinical trials
6	Collection of real-world big data through cardio-oncology registries and quality improvement studies
7	Using high quality data to support implementation and scale-up and establish cardio-oncology guidelines for adults
8	Co-designing studies and innovations with consumers, carers, health care professionals, community-based organisations, and policy makers to reduce barriers and ensure health equity

improvement studies; (7) using high-quality data to support implementation and scale-up and establish cardio-oncology guidelines for adults; and (8) co-designing studies and innovations with consumers, carers, health care professionals, community-based organisations, and policy makers to reduce barriers and ensure health equity. These strategies cover the entire research pipeline and sequentially can ensure that important fundamental discoveries are translated to clinical use, policy, and practice. It is also important to delineate differences and similarities between adult and paediatric cardio-oncology practices and care, and to aim for better research alignment between paediatric and adult cardio-oncology. Only through a combination of these strategies are we likely to achieve sustained improvements in CV health for people living with and beyond cancer. The ACvA and its flagships are ideally placed to fulfil these priorities, and provide the advocacy needed to expand and advance the field.

In Australia, CVD is a common cause of mortality and morbidity during and after cancer treatment. Australia has established cardio-oncology clinics, research across the translational pipeline, and professional networks, which will continue to gain traction as awareness and funding grow. At the core, multidisciplinary research and clinical collaborations, including consumer representatives, will be key to breaking down silos and improving care coordination among cardiology, oncology, primary care and other health professionals, patients, and carers. Moreover, leading advocacy bodies have established cardio-oncology as a priority area for research and patient care, and several national medical organisations have established cardio-oncology working groups to promote evidence-based research solutions. The ACvA flagships provide an example of how high quality research by multidisciplinary teams across the translational pipeline can support delivery of novel strategies for reducing risks of cardiotoxicity during cancer treatment and improve CV outcomes. Together, these strategies will improve high quality cardio-oncology research and care, and drive new guidelines, policies, and government initiatives to ensure equity in health outcomes for all cardio-oncology patients in Australia.

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Conflicts of Interest

The authors are members of the Australian Cardiovascular Alliance (ACvA). K.D. is the CEO of the ACvA and G.F. was the ACvA President at the time of manuscript preparation and submission.

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Author Contributions

A.C.S., A.L.S., D.T.M.N., and J.R. conceived and drafted the manuscript. All authors have read, provided feedback, revised, and approved the final manuscript.

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