



# The Australian Cardiovascular Alliance— Towards an Integrated Whole-of-Nation Strategy to Address Our Major Health Burden

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## Introduction

The health and societal burden of cardiovascular (CV) disease is massive. It is already the most costly to the nation approximately \$8.8 billion each year of direct health costs alone [1], and this is predicted to grow [2]. Australia has an admirable health system and a well-deserved reputation for the quality of its health and medical research. However, this coming tsunami of CV disease will test the resilience and effectiveness of our research governance and our historical funding allocation frameworks. We need to develop innovative pathways that ensure all Australians receive best evidence-based care, as well as ensure that new treatments, and diagnostic techniques cross the challenging translational valleys “of death” to benefit our patients, and that the missing biology of common complex disease is unravelled.

The Australian Cardiovascular Alliance (ACvA) is a not-for-profit, incorporated entity, established in 2015 by founding board members Jaye Chin-Dusting, Stephen Nicholls, Tom Marwick, Robert Graham, Kerry Rye, Livia Hool and Jonathan Gollidge. The ACvA aims to increase the visibility of CV disease as a National Health Priority Area with the general public. Our primary activities involve advocating for increased peer-reviewed funding for research into heart, stroke and vascular disease and promoting the development of strong collaborative networks between CV researchers

nationally. We have rapidly grown to become a comprehensive collaboration of our highest quality cardiovascular research bodies and scientific societies, individual researchers, industry and non-government organisations, and are committed to work with Federal and State governments towards a solution. Formally partnered with the Heart Foundation, the ACvA is uniquely positioned to leverage key interactions between our strong research capability and the health system to improve health outcomes and reduce costs. Deep engagement of our members with the local health districts and primary care, including via the National Health and Medical Research Council (NHMRC) and Advanced Health and Research Translational Centres (AHRTCs) provides opportunities for coordinated whole-of-nation, and whole-of-pipeline approaches to tackle our greatest disease challenge (Figure 1). However, strategic investment is required.

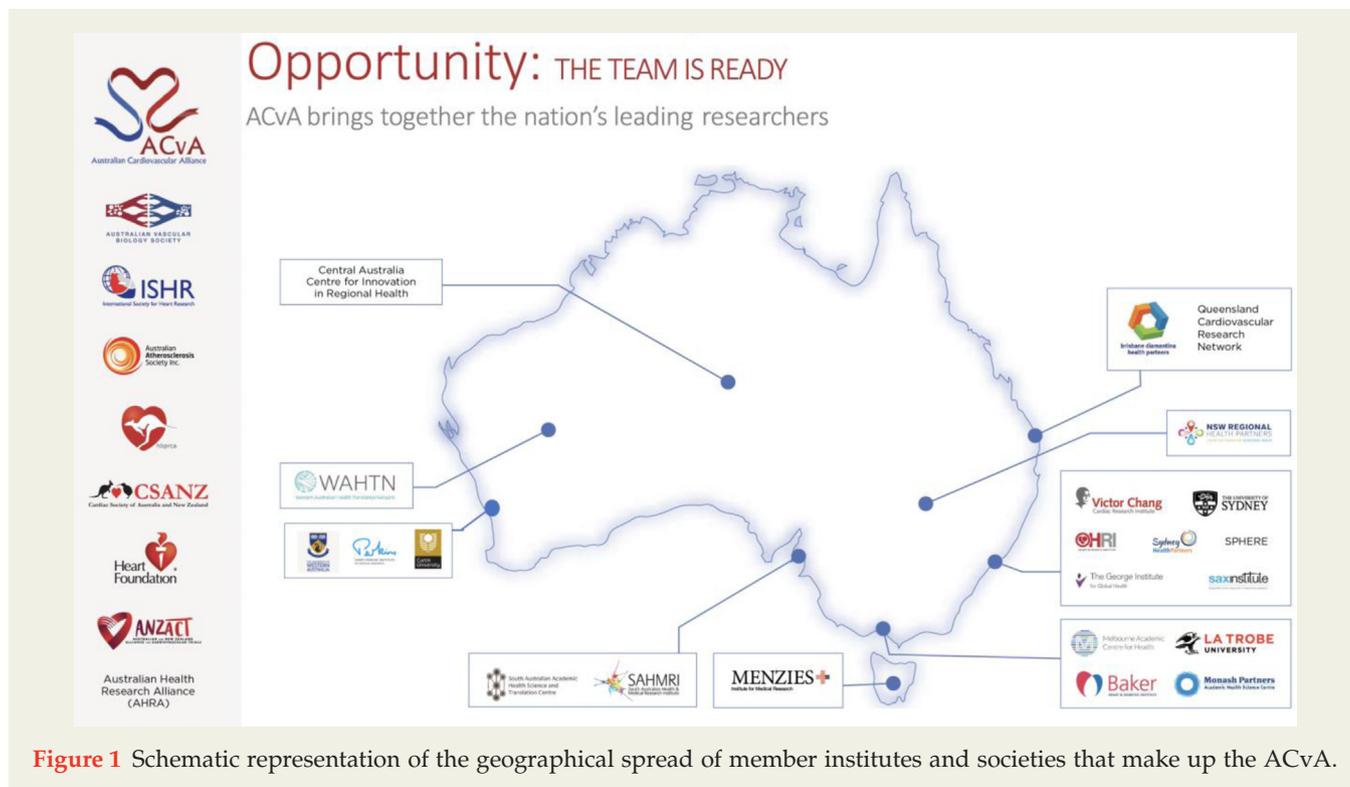
## Capacity and Funding Challenges

Australian medical researchers are recognised internationally for their ongoing contributions to the CV field, from fundamental biological discoveries to large scale clinical trials and implementation of life-saving public health policies. However, these discoveries and successes have occurred in “siloes” fashion, with the CV research community being shrunk down to small, high quality pockets in

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response to funding stress. Talented early and mid-career researchers have been attracted away to alternative fields, or to international centres of excellence. The current levels and schemes for funding are a disincentive for new researchers and clinicians to enter the field of CV research, and are not supporting the collaborative effort required to tackle the future burden of CV disease. An over-arching, Federally supported strategy will help transform fundamental discoveries of new biomarkers of early risk; of new therapeutic targets and drug development; and of bioengineering inventions that are not able to easily to “make” it across the “translational gap” to first in human, early phase clinical trials, and beyond into evidence-based implementation.

An additional problem for CV research has been the community and government perception that the pathology is all understood, and those that suffer from heart disease do so through poor choices in lifestyle, or as an inevitable result of ageing. The mechanisms underpinning why one person is susceptible, and another resilient provide the answers for improved preventative and treatment strategies. The community perception of cardiovascular disease has led to substantial differences in both Federal and charitable investment in CV versus cancer research, with cancer research receiving at least 10 times more funding from government agencies and charities compared to CV research (Figure 2). This difference is associated with game-changing discoveries and improved life expectancy for cancer patients.

### New Strategic Funding Opportunities

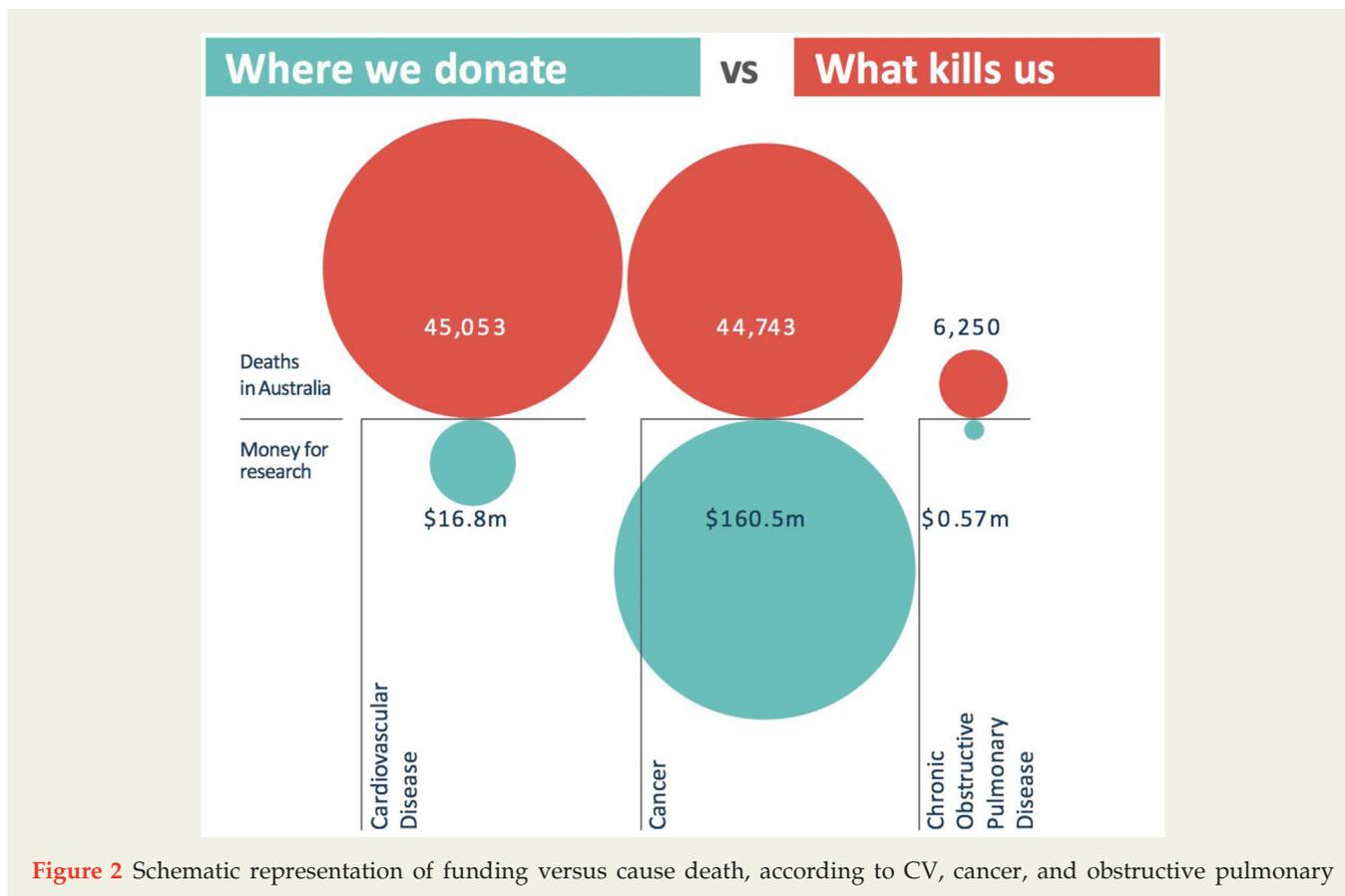
The NSW Government can be commended for its vision in committing \$150 million to cardiovascular research over 10

years, recognising both the importance in tackling the disease burden, but also the potential for commercial and economic gain. This was the culmination of a long-standing dialogue and effort between the NSW Cardiovascular Research Network, the NSW Office of Health and Medical Research, and a specific business case led by Professors Bob Graham (Executive Director, Victor Chang Cardiac Research Institute) and Shaun Jackson (Director, Heart Research Institute), and Mr Matthew Grounds (UBS Australia chief executive).

The Federal Government's investment in the Medical Research Future Fund is an additional opportunity for strategic injection of funds into a capacity-challenged cardiovascular research sector and has the potential to change the face of Australian health. The key components of the *Medical Research Future Fund Act 2015 (Cth)* that the Australian Medical Research Advisory Board (AMRAB) is required to consider when determining the priority for distribution of funds are very relevant to an argument to support Cardiovascular Research and include:

1. Burden of disease
2. Delivery of practical benefits from research and innovation to as many Australians as possible
3. Complementary and enhancing impact of MRFF investment with other financial assistance.

Whilst a number of different schemes have emerged from the MRFF to support ground-breaking Australian research, the ACvA believe that the most appropriate model to tackle the burgeoning challenge of CV disease is that of a Medical Research Mission. This is described as a program of work with “ambitious objectives that are only possible through



**Figure 2** Schematic representation of funding versus cause death, according to CV, cancer, and obstructive pulmonary

significant investment, leadership and collaboration". It is the leadership and collaboration that distinguishes it from other models, that is required along with funding to ensure we rapidly increase capacity, reversing the brain drain; accelerate discovery; enhanced translation and industry investment; and, ultimately, improve the health of Australians. A saving of just 2% of the direct economic costs of cardiovascular disease would bring a saving of \$172 million per annum.

### Atherosclerosis—A Case in Point

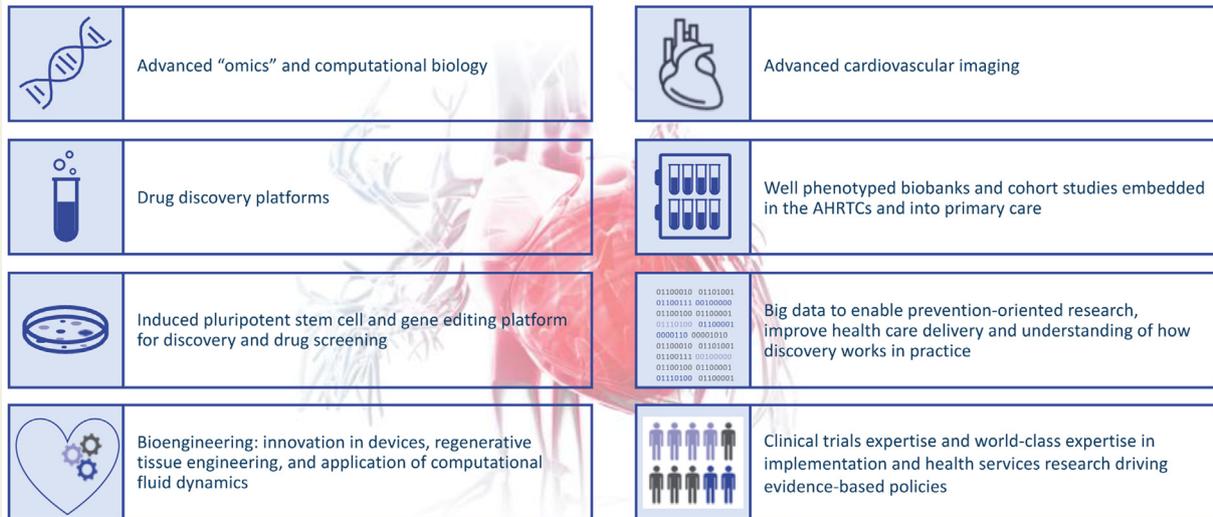
Atherosclerosis is one example of one of our greatest health challenges that requires a coordinated effort that would be catalysed by such a Mission. We have achieved dramatic reductions in cardiovascular morbidity and mortality through identification and targeting of major modifiable risk factors for atherosclerosis in the community, including smoking, high blood pressure, diabetes, and high cholesterol, and in the acute interventional management of heart attack and stroke. Further efforts and novel approaches for community engagement are required in this regard, based on evidence from our global leaders (e.g. The George Institute (Sydney, NSW, Australia), The Sax Institute (Sydney, NSW, Australia)). Indeed, sobering evidence demonstrates that 1.4 million Australians aged 45-74 have greater than 15% absolute risk of CV event in the next 5 years, but only 30% of these are receiving appropriate preventative therapy [3]. Research and improved implementation of existing

guidelines will help to reduce the incidence and individual impact of heart attack, stroke, peripheral vascular and renal disease. However, these factors only address part of a complex equation. Each individual has a unique biological response to the same environmental or metabolic "attack", which is an important factor in their susceptibility to atherosclerosis.

Whilst continuing to address the factors "attacking" the artery through public health strategies for improved lifestyle and uptake of evidence based primary pharmacotherapies, we need to combine our efforts to understand individual variation in susceptibility to disease. The timing has never been better to bring together biobanks from large, well phenotyped cohorts, and apply state-of-the-art multi-omic analysis to discover new markers for early disease, and new therapeutic targets. Aligning this with clinical follow-up and linked data will be a very powerful asset for discovery. An aligned strategy across CV research and translation is required to ensure such discovery makes the journey back to the clinic, with new markers and therapies tested and implemented. This will have important benefits in reducing the burden of heart attack, stroke, peripheral vascular and kidney disease. This should be seamlessly integrated, in a bidirectional manner, with ongoing efforts at public health and community levels.

Investing in a nation-wide strategy for CV research is timely, as highlighted by the strengths that we have across the country (Figure 3). It will apply our strengths in

World class technology platforms and expertise that will be maximised by strategic funding and coordinated national CV research strategy.



**Figure 3** The timing is right. We have the expertise to tackle the missing biology in cardiovascular disease, providing new early markers of disease, and opportunities for improved preventative and therapeutic strategies.

fundamental research and state-of-the-art multi-omics technologies to well-coordinated patient cohorts and biobanks, and work with increasingly deep electronic linked datasets. This will allow for new discoveries into the underpinnings of disease pathophysiology and unique, patient-specific susceptibility to cardiovascular disease. Moreover, by integrating efforts into a bi-directional pipeline that builds iteratively from active laboratory to clinic interactions, and back again, this whole-of-nation approach will provide new mechanisms and markers for detecting early disease, as well as novel therapeutic targets for drug discovery that can be rapidly advanced to clinical trials and improved health outcomes. Strengths in implementation science and policy, will also benefit an effort to ensure that evidence-based care is available and appropriately delivered to all Australians in need.

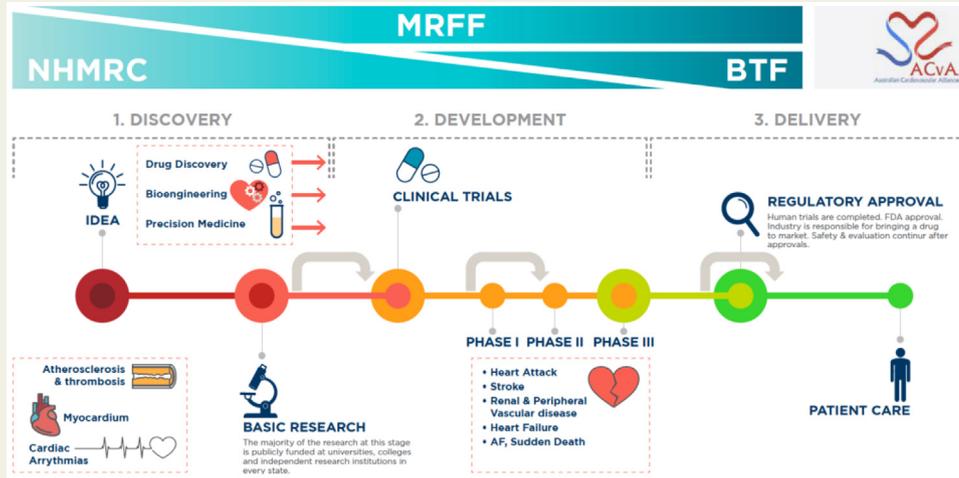
We propose investment in a whole-of-nation approach that addresses current gaps in the translational pipeline to maximise our impact (as illustrated schematically in [Figure 4](#)). After extensive consultation both internationally, and across the country, the ACvA have devised six strategic flagships that could be the centrepiece of a Mission and would provide a platform of our strengths in research and clinical care to be leveraged optimally: 1) *Implementation research and policy*; 2) *Clinical trials*; 3) *Big data*; 4) *Precision medicine*; 5) *Drug discovery*; and 6) *Bioengineering*, applied to cross-cutting themes of atherosclerosis, heart muscle disease, and cardiac arrhythmias. Capacity building initiatives will be instituted at the preclinical/clinical interface- with large, well-phenotyped cohorts and biobanks funnelling opportunities for de novo discovery, and preclinical discoveries and innovations being identified and prepared for early phase clinical trial. Investment in bioinformatics would benefit all flagships.

## Impact for Australia

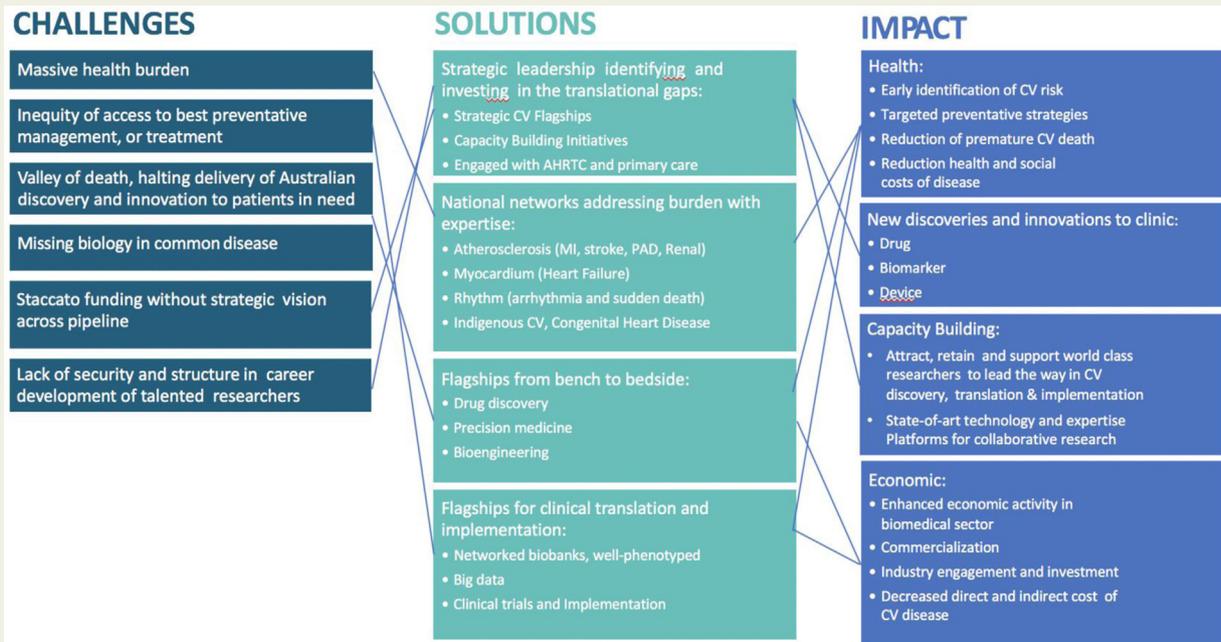
Historically, medical research in Australia has delivered strong health and economic benefits, with recent analysis demonstrating a benefit-to-cost ratio of 3.9, based on health gains and wider economic gains from a larger and more productive population and commercialisation of medical research. Cardiovascular research has delivered the highest returns on investment for chronic conditions, with a benefit-to-cost ratio of up to \$9.8 for every dollar invested [4]. An investment logic model is provided in [Figure 5](#), addressing the challenges, solutions and potential impact of investing in the Australian CV Research sector.

Strategic investment in a nation-wide coordinated CV research program will return the following benefits to Australia:

1. Improved health: e.g
  - Higher proportion of patients identified at risk, receiving appropriate primary prevention.
  - Healthier ageing: reducing premature death and disability from heart attack, stroke and heart failure.
  - Cleverer prevention: earlier detection of subclinical atherosclerosis, reducing the number of patients presenting with heart attack or stroke as their first knowledge of disease.
  - Improved outcomes for heart attack patients, with less heart muscle damage, shorter hospital admissions, and less secondary heart failure.
2. Capacity building and reversal of brain drain:
  - Investment in CV disease research, in a manner appropriate for disease burden, alignment of research skills to health problem, and our research skills will allow for the growth of a true cardiovascular research and clinical industry to be built in Australia.



**Figure 4** Schematic representation of a “whole-of-pipeline”, national CV research program that would invest in 6 Strategic CV Flagships- Implementation and policy, Big data, Clinical Trials, Precision Medicine, Bioengineering and Drug Discovery, driving new discoveries, treatments, and policies.



**Figure 5** Investment logic model, outlining the challenges, solutions and likely health, research, and economic impacts.

- Shared platforms applying state-of-the-art technology, including for drug discovery, and multi-omic molecular phenotyping.
- National registries and biobanks.
- Harmonised approaches to “big data”.
- Attracting international rising and “risen” stars to Australian soil.
- 3. Commercialisation:
  - Cardiovascular pharmaceutical and device companies are a major strength in the global biotech sector. The ACvA include Siemens, Astra Zeneca, Boehringer

- Ingelheim, Medtronic, Sanofi as members, and have major goals that include increased industry engagement and translation of evidence-based diagnostics and therapeutics to the Australian population to improve health.
- A collaborative whole-of-pipeline platform, with appropriate investment, will make Australia an attractive place for industry to position its discovery, translational and implementation research.
- Investment in CV research is highly likely to improve commercialisation outcomes and catalyse a thriving

pharma/bio-tech sector with enhanced development of new spin-off biotech companies and engagement between industry and academic CV research.

4. Financial benefits:
  - Reduction in direct health care costs (at \$8.8 billion per annum, a 1% reduction brings \$88 million saving)
  - Enhancing productivity
  - Thriving biotech industry, bringing international investment

## Conclusion

The Australian CV research community is historically well-positioned, with united commitment from key stakeholders, to work with the Federal Government, as well as State governments, local health districts and primary care jurisdictions, towards an integrated strategy to combat cardiovascular disease and its devastating impacts.

For further information regarding the ACvA and its activities, please see <https://www.ozheart.org>

## Acknowledgements

We particularly acknowledge the enormous efforts of Ms Britt Granath and Mr Matthew Grounds, as well as members of the Board, and members of the ACvA.

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