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Boosting musculoskeletal research through strategic co-investment with the Medical Research Future Fund

2017/18 Pre-budget submission

About Arthritis Australia

Arthritis Australia is the peak arthritis organisation in Australia and is supported by affiliate offices in ACT, New South Wales, Northern Territory, Queensland, South Australia, Tasmania and Western Australia.

Arthritis Australia provides support and information to people with arthritis as well as their family and friends. It promotes awareness of the challenges facing people with arthritis across the community, and advocates on behalf of consumers to leaders in business, industry and government.

In addition, Arthritis Australia funds research into potential causes and possible cures as well as better ways to live with the disease.

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Overview

Purpose

To seek co-investment from the Medical Research Future Fund (MRFF) for initiatives which align with MRFF strategies and priorities and which build much needed research capacity in the National Health Priority Area (NHPA) of arthritis and musculoskeletal conditions.

Funding sought: $7.6 million over five years comprising:

- $2.6 million to match funding from Arthritis Australia's research program for Clinical Researcher Fellowships
- $1.5 million for infrastructure funding for the newly established Australia and New Zealand Musculoskeletal Clinical Trials Network
- $3.5 million to augment philanthropic and partner contributions, to enable nation-wide rollout of the Australian Arthritis and Autoimmune Biobank Collaborative (A3BC).

This is a modest level of funding, accounting for less than 5% of total funds available for disbursement from the MRFF in its first two years, for a group of conditions that account for 12% of the total burden of disease and injury in Australia.

Rationale

Strategic investment from the MRFF will help to address the critical issue of limited research capacity and funding in the area of arthritis and musculoskeletal conditions in Australia.

Research funding for musculoskeletal conditions is disproportionately low relative to the disease burden and cost of these conditions.

These conditions account for 12% of the total disease burden and 8% of disease expenditure (third most costly NHPA), and are the leading cause of chronic pain, disability and early retirement due to ill-health. Population ageing, growing obesity levels and increasing rates of autoimmune conditions will see a substantial increase in this burden and cost in future.

Yet this NHPA receives just 3.5% of NHMRC research funding for NHPAs, equal lowest with asthma, and funding levels are declining.

Ongoing low levels of research funding have severely undermined research capacity, with serious implications for future research and for sustaining clinical excellence in the field.

The proposals outlined in this submission will boost research capacity and are expected to achieve a quantum leap in the quality and utility of research in the musculoskeletal field.

The proposals align closely with the strategies and objectives of the MRFF as they will: support collaborative, innovative and translational research; build infrastructure and harness data to enable personalised medicine; and support research which addresses evidence-practice gaps in health services.

They also provide an opportunity to co-invest with, and leverage funding from, the philanthropic sector for MRFF strategies and priorities.

The case for investment

By any metric, be it disease burden, cost, prevalence, disability, quality of life or productivity, there is an urgent need to prioritise research on the most effective and affordable strategies to deal with musculoskeletal conditions.

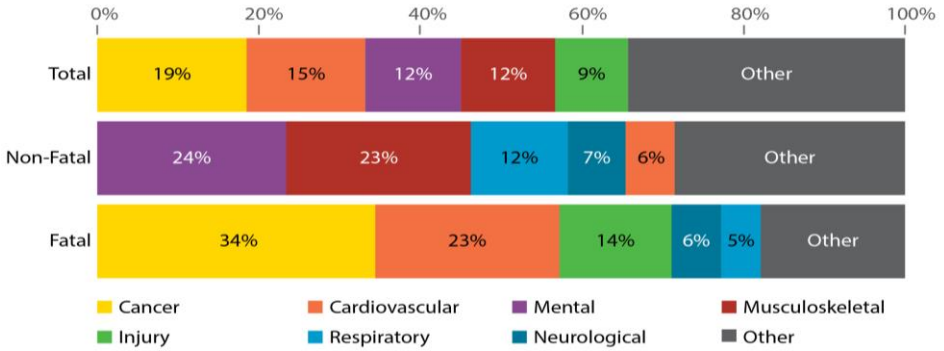
High burden, high cost conditions

Arthritis and musculoskeletal conditions is group of conditions which includes over 100 forms of arthritis and other conditions such as back pain. These conditions are

- The most common and disabling of all chronic conditions, affecting nearly 7 million[1] people of all ages and accounting for at least 31% of disability[2]
- The fourth leading cause of total disease burden in Australia, accounting for 12% of the total burden and 23% of the non-fatal burden (Figure 1)[3]
- The third most costly NHPA, with health system costs of $5.7 billion in 2008-09 (9% of disease expenditure) (Figure 2) [4]
- A major drain on economic productivity as the leading cause of health-related early retirement, at an annual cost of $15 billion in lost GDP alone (Figure 3).[5]

Population ageing, growing obesity levels and increasing rates of autoimmune conditions will see a substantial increase in this burden and cost in future.

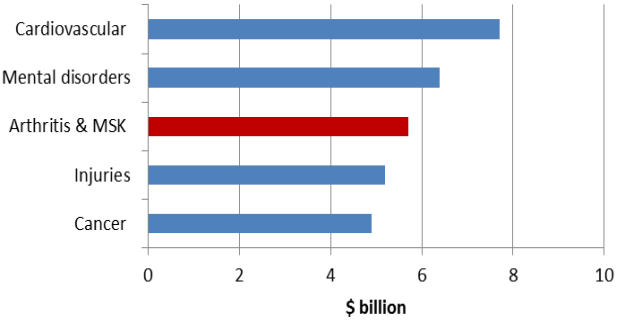
Figure 1: Proportion (%) of total, fatal and non-fatal burden by disease group, Australia, 2011



Source: AIHW[3]

Figure 2

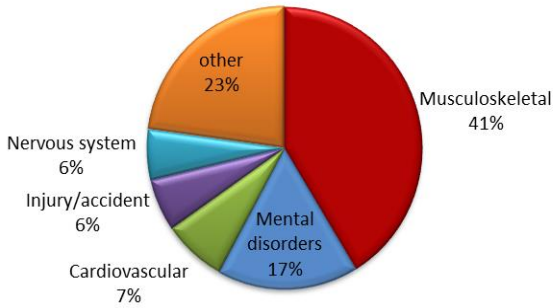
Health system expenditure 2008/09 - top five National Health Priority Areas



Source: AIHW[4]

Figure 3

Main chronic conditions - people aged 45-64 yrs not in labour force due to ill-health, 2010



Source: Schofield et al 2015[5]

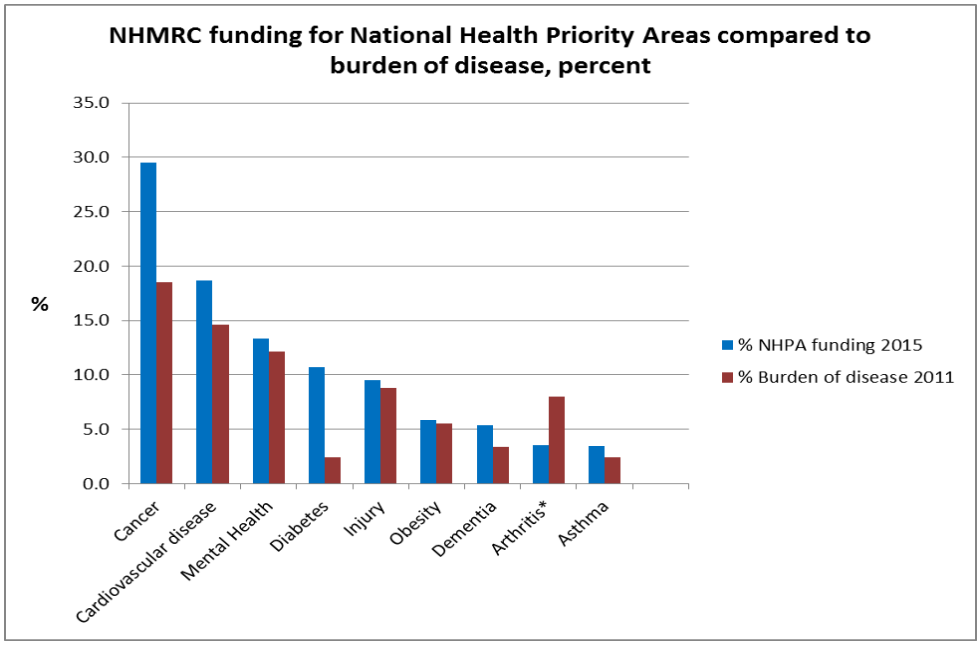
Disproportionately low research funding

Research funding for musculoskeletal conditions is disproportionately low relative to the disease burden and cost of these conditions.

- NHMRC research funding is generally considered to align with disease burden. In 2015 however funding for the musculoskeletal National Health Priority Area was just 3.5% of total NHPA funding, or around one quarter of the estimated disease burden of 12%.[6]
- In contrast relative funding is higher than the disease burden for every other NHPA (Figure 4)

Low levels of research funding are severely undermining research capacity, with serious implications for the future of arthritis and musculoskeletal research in Australia and for the ability to sustain clinical excellence in the field.

Figure 4



* Burden and funding based on arthritis and osteoporosis only as these are the focus areas of the NHPA
Source: NHMRC website[6]

Substantial scope for research to improve care and save costs

Much money is spent on care for people with arthritis and musculoskeletal conditions which is inappropriate, unnecessary or has an inadequate evidence base. Some areas of expenditure where research could achieve substantial cost savings include:

- **$400 million** a year spent on biological drugs for rheumatoid arthritis,[7] which could be spent more effectively with research to improve drug targeting
- **$170 million** a year spent on knee replacements that could be avoided with lifestyle modifications[8] (total cost of knee replacements - $1.2 billion[9])
- ***$90 million*** a year spent on surgery for wrist fractures in the elderly[10] without adequate evidence of additional benefit compared to non-operative care
- ***$220 million*** a year on imaging for low back pain,[11] which may be mostly unnecessary.[12]

Proposals

1) Co-invest in Clinical Researcher Fellowships

Proposal

Co-invest in Clinical Researcher Fellowships through Arthritis Australia's National Research Program.

Funding sought: $2.6 million over five years

Rationale

Clinician researchers play a critical role in clinical problem solving and in fostering faster translation of research into clinical practice.

However, clinician researchers in the area of arthritis and musculoskeletal conditions are scarce. There are currently only two NHMRC funded Practitioner Fellowships in musculoskeletal research. Limited research funding and capacity in the field means that few musculoskeletal researchers have the track record to be successful under the Practitioner Fellowship Scheme.

There is an urgent need to support clinician researchers in arthritis and musculoskeletal conditions to identify and address the many issues and uncertainties relating to providing care for people with these conditions.

About Arthritis Australia's Research Program

Arthritis Australia is the largest non-government funder of research into arthritis and musculoskeletal conditions in Australia. In 2016 we allocated $900,000 towards research.

Our national research program funds the breadth of research from basic laboratory research designed to understand the mechanisms of disease, through to clinical projects undertaken to investigate and improve quality of life for people with musculoskeletal disease.

An important objective of our research program is to foster early career researchers to assist in building much needed research capacity in the field and to help them achieve a track record so they can successfully apply for NHMRC funding.

Supporting clinical researcher fellows

Arthritis Australia is keen to foster clinician researchers in Australia, especially early career researchers as this will help to build research capacity in the field.

Arthritis Australia proposes to allocate $525,000 a year over the next five years through its research program, to fund clinical researcher fellows in the field. This will fund seven (7) part time clinical researcher fellows of varying seniority each year.

We seek an equivalent co-investment from the MRFF to double the impact of this program.

Alignment with MRFF priorities

This proposal aligns directly with the MRFF priority of expanding the scope and scale of clinical researcher fellowship programs.

2) Infrastructure funding for ANZMUSC Clinical Trials Network

Proposal

Provide infrastructure funding from the MRFF for the Australia and New Zealand Musculoskeletal Clinical Trials Network (ANZMUSC).

Funding sought: $1.5 million over four years.

Rationale

Clinical trials networks are networks of volunteer clinicians and researchers who undertake investigator-initiated trials designed to address clinically important questions which are directly related to optimising outcomes for patients and the health system.

Investigator driven clinical trials activity in the musculoskeletal field is currently hampered by limited research capacity and funding. NHMRC funding for musculoskeletal clinical trials is just 5% of total NHMRC clinical trial funding which is proportionately low compared to the burden and cost of these conditions.

To address this issue, ANZMUSC has been recently established to improve clinical research quality and capacity in the field and to address key clinical questions for the most common musculoskeletal conditions. It is the first formal clinical trials network in the field.

Trials already commenced by ANZMUSC address a number of high-expense, limited-evidence clinical issues including:

- Reducing inappropriate imaging for back pain
- Determining the effectiveness of expensive surgery for lumbar spinal stenosis.
- Assessing whether surgery for wrist fractures in the elderly offers any additional benefit compared to non-operative care.

The potential savings from research in these areas total many millions of dollars a year.

Because ANZMUSC, like other clinical trials networks, is primarily run by volunteers, infrastructure funding is essential to underpin its successful operation.

MRFF investment in ANZMUSC infrastructure is likely to be recouped many times over in massive longer-term savings for the health system.

About ANZMUSC

ANZMUSC is a newly established collaboration between leading clinician-researchers across a range of disciplines relevant to musculoskeletal research and health consumers, including Arthritis Australia. Its vision is to optimise musculoskeletal health through high quality, priority driven, collaborative clinical research.

ANZMUSC will facilitate the conduct of large-scale clinical trials to answer the most critical questions for common musculoskeletal conditions. By focusing on large evidence and evidence-practice gaps, ANZMUSC research will support more cost-effective and evidence-based care for people with these conditions, with the potential for significant long-term savings for the health system.

ANZMUSC will

- Generate new knowledge that leads to improved health outcomes
- Promote effective transfer of research outcomes into health policy and/or practice
- Develop the musculoskeletal health and medical research workforce
- Facilitate collaboration between clinicians, researchers, consumers, policy makers.

Alignment with MRFF strategies and priorities

Providing infrastructure funding to ANZMUSC aligns with a number of MRFF priorities.

- **Clinical trial network**

This funding request directly aligns with the MRFF priority of providing infrastructure support for existing and new national clinical trial networks.

- **International collaborative research**

ANZMUSC includes members from both Australia and New Zealand. A number of ANZMUSC members are global leaders in their research field and can harness their international connections outside Australasia as well to support international collaborative research.

- **Clinical researcher fellowships**

ANZMUSC plans to support six (6) part-time clinical research fellows to address priority research questions identified by the network. Three of those positions would be funded through an NHMRC Centre of Research Excellence grant (if successful) and the remainder by the network's industry and professional association partners.

- **Building evidence in primary care**

A number of procedures for musculoskeletal conditions funded under the MBS have an inadequate evidence base to support their effectiveness or cost-effectiveness. ANZMUSC members are already working with the MBS Review Taskforce to identify interventions with limited supporting evidence.

Through its priority setting process, ANZMUSC will identify those areas of research related to MBS funded procedures which are likely to generate the greatest impact and return on investment.

Funding

ANZMUSC was formed in 2015 with a small amount of seed funding donated by stakeholders.

Funding is also being sought from NHMRC to establish a Centre of Research Excellence (CRE) for the Network.

Infrastructure funding is not covered by the NHMRC but is urgently required to support the operation and growth of ANZMUSC. The requested infrastructure funding would cover the cost of an Executive Officer, office, administrative support and communication/meeting costs for the network.

3) Co-invest to enable the nation-wide roll out of the Australian Arthritis and Autoimmune Biobank Collaborative (A3BC)

Proposal

Provide $3.5 million over five years from the MRFF to augment philanthropic donations and partner contributions for the development and nation-wide roll out of the Australian Arthritis and Autoimmune Biobank Collaborative (A3BC).

Rationale

Biobanking is becoming an increasingly important research tool, with up to half of new medicines in clinical development being personalised medicines which rely on biomarker data provided by biobank collections.[1]

The A3BC will be Australia's first national biobank network for arthritis and autoimmune conditions. This important shared resource will provide world-class biobanking and big data modelling to enable accelerated research into biological ('omics') and environmental risk factors associated with these costly and debilitating conditions.

The A3BC will be an invaluable resource for researchers and a major enabler of personalised medicine. In particular, it will foster national and international research to identify and understand disease biomarkers related to the onset and progression of these conditions. Such discoveries will enable safer, more cost-effective targeting of existing therapies, such as expensive biologic medicines, and the development of new therapies.

The A3BC aligns closely with the objectives, strategies and priorities of the MRFF. It will: provide valuable data and infrastructure to support researchers; drive collaborative and innovative research; foster transdisciplinary, national and international collaboration, support data linkage and analysis; and build research capacity in new fields such as genomics and bioinformatics.

Seed funding for the A3BC has been provided through a major philanthropic grant and a number of partners have pledged additional funding and in-kind contributions. This will allow a limited, staged rollout of collection sites.

Additional funding is sought from the MRFF to support and accelerate the nation-wide roll out of the A3BC.

A3BC objectives

The objectives of the A3BC are to:

- Collect biospecimens (eg blood and tissue samples) from people with arthritis and autoimmune conditions using a national 'hub and spoke' network with collection sites in major tertiary hospitals in every state.

  Biospecimens will be collected at different disease stages to provide longitudinal data to assess relationships between biological and clinical factors over time.

[1] Tufts Center for the Study of Drug Development. Personalized Medicine Is Playing a Growing Role in Development Pipelines. Impact Report, 12 (November/December 2010): 6.

- Integrate biobank samples with the Australian Rheumatology Association Database (ARAD) and other databases to allow linkage with health, lifestyle and clinical follow up data. This will exponentially boost the value of biobank collections.

  ARAD is a national registry which collects comprehensive disease, therapy and quality of life data from thousands of patients. It also links with Medicare and Pharmaceutical Benefits data, cancer and joint replacement registries and patient medical histories, to enable assessment of outcomes and health services utilisation.

- Develop epigenetic research in the field via state of the art technologies in big data modelling, in collaboration with leading national and international universities, to unlock world-leading basic and clinical research capacity and capabilities.

A3BC development and rollout

Work has recently begun to establish the A3BC, which is being developed with the unanimous support, collaboration and/or partnership of key national stakeholders, including health practitioners, researchers, consumers, service providers and industry.

Integration and linkage with existing biobanks and databases, including the CLARITY biobank for juvenile arthritis (Murdoch Children's Research Institute), are planned.

The A3BC will adopt international best practices and employ existing State (ie NSW) strategies to embed biobanking within the health system.

Seed funding has been provided through a philanthropic grant to the Kolling Institute for Bone and Joint Research at Royal North Shore Hospital. This grant is for $4 million over 5 years. Additional contributions of cash and in-kind have been pledged by A3BC partners and a sustainable business model, based on industry use, is being developed to drive ongoing revenue. However additional funding is required to support and accelerate the national rollout of the A3BC.

Alignment with MRFF strategies and priorities

The A3BC aligns closely with the strategies and priorities of the MRFF, as outlined below.

Data and infrastructure

Biobanks are essential tools for translational research, in particular genomics and personalised medicine. They are also critical enablers of more efficient and cost-effective clinical trials by allowing improved development from pre-clinical stages to late stage study.

A3BC will provide valuable data and infrastructure for national researchers by providing open access to a repository of biological samples, with linked clinical data, from people with arthritis and auto-immune conditions. This resource will enable and accelerate research and reduce national costs for scientific projects and clinical trials.

In addition, using big data modelling and computational analysis techniques (bioinformatics), A3BC will allow epigenetics, genomics and other 'omics' to be correlated with drug, environment and lifestyle factors to develop disease-specific risk and biomarker profiles, and build novel disease models for drug development.

Two examples of the power of large-scale biobanking in arthritis have been shown by the UK Biobank network which has enabled large-scale studies into phenotypes and comorbidities in rheumatoid arthritis, and into shared genetic pathways linked to cardiovascular, autoimmune, and psychiatric disease.[13] [14]In Australia, the CLARITY biobank for juvenile arthritis is supporting genomic research into a diagnostic test for the condition.

Clinical quality registries

The Australian Commission on Safety and Quality in Health Care (ACSQHC) has identified musculoskeletal conditions as one of the two top priority areas for developing clinical quality registries because of the very high cost and high disease burden of these conditions.[9]

The ARAD database, with its data linkage capability, is well placed to operate as a national clinical quality registry for inflammatory and autoimmune arthritis, in synergy with the A3BC.

Investment in A3BC and its integration with ARAD will enhance the scope and coverage of ARAD by allowing existing ARAD data to be matched with biospecimens and by supporting increased recruitment of clinicians and patients to the database. It will also support enhanced clinical data collection from GPs, rheumatologists, surgeons and allied health professionals to better inform clinical policy and practice. These factors will substantially enhance the value of ARAD as a clinical quality registry.

National data management

Experience with developing the biobank and with data linkage through ARAD, will help to inform any study relating to infrastructure enhancement to expand digitised and linked health and social data. In particular A3BC will demonstrate the potential of data mining and machine learning technologies to discover associations within and between biospecimen data, administrative health data, and clinical data.

The A3BC will expand on recent biobanking work by the NSW State Government and seek to work with the Commonwealth on overcoming data linkage challenges at a national level.

Capacity and collaboration

- ***National collaborative research***

The establishment and roll-out of A3BC will provide an invaluable enabler for increased research capacity and collaboration in arthritis and auto-immune conditions.

A number of partners and collaborators have already committed in principle support for the A3BC and discussions are currently underway with many more entities.

With international best-practice standards and the support of a national network of academics and clinicians, the A3BC has already attracted industry research interest.

- ***International collaborative research***

In parallel with the establishment of national operations, the A3BC will develop existing and new international partnerships with biobanks and researchers in Europe and the United Kingdom to support international collaborative research in the field (see Attachment 1).

Drug effectiveness and repurposing

The A3BC will support more targeted and cost effective drug therapy for people with arthritis and autoimmune conditions by identifying biomarkers which may determine drug effectiveness. This issue is as relevant for the quality use of existing drugs as it is for the development of new drugs.

At present, finding the right therapy for an individual with autoimmune arthritis is a matter of trial and error. There is no clear basis to determine which existing therapies are most likely to work in particular individuals. Individuals may need to try a number of different therapies before they find one that works for them. In addition to the financial cost to the health system, there is a major opportunity cost for patients who have to spend time on ineffective therapies, while their condition progresses and their chance of achieving remission or good disease control diminishes.

Nearly $400 million a year is spent on biologic medicines for rheumatoid arthritis alone.[7] Developing a genetic test to guide drug selection could yield substantial savings in drug and health care costs while improving health outcomes.

Clinical trial networks

The establishment of A3BC will complement and enhance the research output of the Australia and New Zealand Musculoskeletal Clinical Trials Network (ANZMUSC). Together, these two initiatives (A3BC and ANZMUSC) will help to achieve a quantum leap in the quality and utility of research in the musculoskeletal field.

Value of MRFF co-investment

MRFF funding will support the national roll out of A3BC. Additional funding will accelerate the roll out of this collaborative resource and the collection of enough samples and data to drive genomic discoveries.

Currently pledged funding and in-kind support from donors and partners will allow a limited staged roll out of collection sites and the collection and analysis of a limited range of biospecimens in only a few conditions (over 100 conditions could be included).

A co-investment of $3.5 million over five years from the MRFF will enable operational scale-up of the A3BC including:

- More rapid set up of collection and storage sites for biospecimens/samples nationally
- Collection of larger numbers and more types of biospecimens eg articular cartilage in addition to blood, synovial fluid and synovial tissue samples
- Genetic and epigenetic analysis of more samples
- Collection of additional records such as medical imagery (eg X-rays, MRIs).

Further information

Further information on the development and operations of A3BC is available on request.

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