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Submitted to **Medical Research Future Fund consultation to inform the second Australian Medical Research and Innovation Priorities 2018-2020**
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Introduction

1 What is your name?

Name:
Dr Matthew Miles (Multiple Sclerosis Research Australia)

2 Are you affiliated with an organisation?

Yes

3 What kind of organisation do you work for?

Non-government organisation

4 Are you representing your organisation in making this submission?

Yes

5 What state or territory do you live in?

New South Wales

6 Which 2016–2018 MRFF Priorities do you think need further focus? (please select a maximum of three Priorities)

International collaborative research, Public good demonstration trials, Biomedical translation

7 How can the 2016–2018 MRFF Priorities you identified in Question 6 be extended or re-emphasised in the 2018–2020 MRFF Priorities?

How can the most important Priority identified in Question 6 be extended or re-emphasised? (max 500 words):
The biomedical translation priority needs to be expanded to include partnerships with organisations beyond licensed fund managers to enable pre-clinical to early clinical translation of research through matched funding.

Support for pre-clinical work-up of promising compounds and devices would greatly increase translational research activities and the up-take of potential new therapies by industry partners. This is a well-known gap in the Australia research landscape. The priority as it stands is important, but support for pre-clinical to early clinical translation of research would also benefit from the support of collaborations for sourcing matched funding that go beyond partnerships with licenced fund managers, for example with not-for-profit patient-focussed organisations, who often have well established relationships with philanthropists and industry that could also provide novel sources for matched funding. The involvement of not-for-profit patient-focussed organisations will ensure that the research is strongly focussed on improving outcomes for patients.

Funding under this priority should also be extended to include support for other types of network collaborations, such as those where basic researchers, clinicians, and individuals with expertise in industry pre-clinical R&D pathways and processes, regulatory affairs and clinical trials are brought together. Early involvement of industry, regulatory, clinical and clinical trials expertise at proof-of-concept and pre-clinical stages will ensure that product development is targeted, practical and trials are optimally designed to maximise the potential for a successful outcome that will meet the requirements of health technology assessment bodies. Organisations such as the International Progressive MS Alliance, of which MS Research Australia is a managing member, have adopted this model in the development of their strategy and in the funding of major collaborative networks to target translational research for progressive forms of MS. Involvement of an ‘Industry forum’ at all levels of the Alliance’s governance, grant review and collaborative structures has provided invaluable early insight and guidance on the way forward to accelerate solutions for progressive forms of MS that will have the best chance of success once the reach they reach the health technology assessment stages.

If you identified a second Priority in Question 6 please explain how it needs to be extended or re-emphasised? (max 500 words):
The priority of international collaborative research is excellent and should be extended to provide further opportunities in future. Funding under this priority provides opportunities for Australian organisations and researchers to lead international collaborations that will resolve questions that can only be answered by pooling global expertise. The field of MS contains many examples of research that are best tackled with an international perspective, in particular, research into the prevention of MS such as through vitamin D supplementation with, ultraviolet light or a vaccine for one of the MS risk factors - Epstein Barr Virus. Australian researchers are recognised global leaders in both these areas and have performed much of the fundamental research, now is the time to expand this work with international partners to undertake clinical research in people with MS around the world to ensure these findings are delivered to patients. Australia’s expertise and experience in these fields means Australia is ideally placed to lead these global endeavours and work with international partners to achieve the capacity and access to patient sample sizes that are not viable in Australia alone.

This priority should also be extended to include broad and inclusive national collaborations that are also capable of leveraging multiple agency, discipline or industry investment. Collaborative funding ensures outcomes that could not be achieved by researchers acting in isolation and this equally applies at the national level, including focusing attention on patient-centred priorities, furthering translation and implementation of findings, and pooling of expert knowledge, resources and infrastructure. It will also help to avoid research duplication and maximise the mutual use of expensive research infrastructure that may be available in either

the academic sector or the healthcare sector. As an example, MS Research Australia partners with scientists and clinicians around Australia, to coordinate national and international collaborations in areas of research priority to MS. Investment by the MRFF in collaborative efforts such as these at the national, in addition to the international level, would reduce barriers to collaboration and support research and innovation from concept to delivery. Investment in the coordinating body encourages participation and judicious use of funds. As the MS Research Australia platforms have demonstrated, not-for-profit disease-specific organisations are already well positioned to bring together multiple stakeholders, identify patient-centred priorities, and assemble expert collaborators around a common goal.

There is also space for collaboration between different not-for-profits within and across disease areas. To this end, MS Research Australia is also a founding member of the Australian Immunological Alliance. This is a collaboration between a broad range of non-government organisations that have a deep interest in improving the diagnosis, treatment, outcomes, funding, and awareness of immune and autoimmune diseases and disorders. We aim to work together on shared advocacy, awareness and research activities. Recent research has shown there is much overlap between these diseases, especially in genetics, and identified further strategic areas of common research. Expanding this priority to include funding for national collaborations would provide greater opportunities for such cross-diseases, cross-disciplinary ventures.

If you identified a third Priority in Question 6 please explain how it needs to be extended or re-emphasised? (max 500 words):
The public good clinical trials priority admirably covers the extension of clinical trials of proven therapies to at risk groups that would normally not be able to participate and therefore access experimental treatments. This priority needs to be expanded to include clinical trials of medications that are already available for particular conditions but may also be effective for other indications, or over-the-counter medications that may be effective but are untested in a controlled setting. This concept, also covered by the MRFF priority of drug-repurposing, would provide funding for clinical trials that would demonstrate the safety and efficacy of 'off-label' or off patent medications or interventions for potentially high impact, but low-commercial value, therapies that are already licenced or available over-the-counter. This type of research is impossible in the current climate of pharmaceutical industry-led clinical trial funding and at present, especially in the case of over-the-counter medications, patients are self-medicating without robust evidence of the true safety and efficacy of the treatment. Examples of this is the use of vitamin D as a preventative or treatment for MS, or comparative trials of potentially cost-effective, 'off-label' procedures or against the best available approved pharmaceutical therapies.

8 What unaddressed gaps in knowledge, capacity and effort across the healthcare system and research pipeline need to be addressed in the 2018–2020 MRFF Priorities?

Most important gap identified that needs to be addressed in the 2018-2020 MRFF Priorities (max 500 words):
There remains a vital need to embed research into the health system through encouraging the involvement of health care professional (HCPs) of all kinds in research. Involving clinicians at the concept level of research discovery will help to guide the development and rapid translation of research findings into practical and needed interventions. In MS, as in many areas of health, there is the dual problem of research ideas that stem from observations in the clinic, but are never pursued due to time constraints and lack of research capacity in clinicians and the issue of great basic and early clinical research not being translated into patient care. In the field of MS, we have many excellent practitioner researchers and also much of the fundamental research is performed right here in Australia. However, the issue of translation to the clinic persists. This gap could be addressed by the introduction of clinician and researcher paired fellowships and/or nurse and allied health researcher paired fellowships for research.

If you identified a second gap please explain how it needs to be addressed in the 2018-2020 MRFF Priorities (max 500 words):
Further research is urgently required that enables secondary prevention of chronic diseases in susceptible populations. For chronic diseases such as MS, the point of diagnosis is only the start of a journey that involves sustained contact with the health system that continues over a lifetime. For many diseases, including MS, management in the early stages is crucial in determining long term outcomes and often provides a window of opportunity that allows interventions that may slow or stop progression. A diagnosis of MS requires two inflammatory attacks on the brain and spinal cord. People who have only experienced a single attack are given the label "clinical isolated syndrome (CIS)" and individuals can remain in this state for many years or go on to have a second attack and be diagnosed with MS quite quickly. Research into the differences in these people, the effect of lifestyle changes or other interventions, early access to treatments usually given to people with MS is urgently required to try to prevent conversion to clinically definite MS. For a lifelong disease such as MS, this type of research would provide the dual benefit of delivering better health outcomes for patients by keeping them at a stage of their disease with fewer symptoms and overall disability and additionally provide an immense cost saving to the Australian health system through lower health, disability, lost productivity and care costs of the population.

If you identified a third gap please explain how it needs to be addressed in the 2018-2020 MRFF Priorities (max 500 words):
Research to enable early diagnosis and early intervention in chronic conditions is critical to ensure the best possible outcomes for patients and is also a more cost effective way of treating chronic illnesses in the population. Streamlining the care pathways through the health and disability systems is vital to ensure that time is not lost and access to treatment improved. However, funding for research is needed to determine the optimal way to deliver outcomes for many chronic diseases, including MS, in the Australian system. As above, this research will provide the twin benefits of reducing the burden of disease on patients and society and reduce the cost to the health system.

Further research is also needed into the delivery of care for patients with chronic diseases. For example, in MS, more research is needed to conclusively demonstrate the benefit of multidisciplinary teams in the treatment of disease and the benefit of MS nurses in the clinic. Funding for basic and applied research in this area would provide much needed evidence to create change and improve the health care experience and quality of life for people with chronic diseases.

9 What specific priority or initiative can address the above gaps?

What specific priority or initiative can address the first gap identified in Question 8? (max 500 words):
There remains a vital need to embed research into the health system through encouraging the involvement of HCPs in research. Involving practitioners at the concept level of research discovery will help to guide the development and rapid translation of research findings into practical and needed interventions.

Also identified as a priority area in the McKeon Review, further funding needs to be made available for pairs of clinician-researchers working on a common research project. This could take the form of clinicians paired with researchers, or nurses or allied health practitioners paired with allied health researchers. This type of funding gives clinicians the space to complete research within their busy schedules and also provides efficient mentoring and training of HCPs in research skills and ensures that the research is completed to a high research standard with help from experts in specific methodologies or analysis techniques.

As an example, MS Research Australia has launched a fellowship scheme that pairs a clinician and researcher to collaborate on research and implement findings at a clinical level. In its inaugural year, this fellowship pair was awarded to a senior clinical neurologist and senior researcher working in myelin repair. The funding will allow the outcomes of the myelin repair work to be fast-tracked into clinical trials for people with MS and concurrently take a clinical finding from families with MS back to the laboratory to determine the underlying cellular mechanisms.

Equally, clinical research gaps are often identified by nurses and allied health practitioners, but the capacity within the health system for nurse-led research is limited. Fellowships that fund nurses and allied health researcher pairs would similarly provide the stimulus to carve out time for this important research by nurses and provide rigour to the research design. MS Research Australia recently held a workshop on the role of modifiable lifestyle factors in MS. This workshop identified that counselling and delivery of advice to people with MS about modifiable lifestyle factors needs further research, not least due to disease-specific barriers including cognitive symptoms and fatigue. However, it was also noted that the capacity of the already stretched clinical nurses was limited. Funding of a nurse-allied health researcher pair would alleviate part of this pressure.

If you identified a second gap in Question 8 what specific priority or initiative can address this gap? (max 500 words):
Research into secondary prevention for people at the earliest stages of chronic disease is essential to ensure the best possible outcomes for patients and reduce the burden on the health system and on society. Funding for range of areas could be considered under a priority of secondary prevention.

Firstly, funding for basic research into the factors that slow or halt chronic diseases, including lifestyle or other modifications, such as managing comorbidities, is urgently needed to determine the ways that diseases worsen and progress over time. For example, in MS, research has already shown that factors such as smoking and exercise play a big role in the progression of the disease. Adopting a brain healthy lifestyle including a healthy diet, staying physically and mentally active as well as avoiding smoking and limiting alcohol can all improve outcomes in MS. But further research is still needed, for example, to identify what is the optimal diet for this specific condition, or the optimal type and dose of exercise. These types of clinical study would then underpin evidence-based advice given to patients at the clinic about steps they can take to slow the progression of their disease. At present, there is a huge amount of interest from the MS community about things that they can do themselves to improve their disease outcomes, but the scientific evidence is lacking. This situation is mirrored across the spectrum of chronic diseases. Patients need to be empowered with good evidence-based advice but this requires investment in research.

Another area that would benefit from funding is research into the way that this advice needs to be translated to the clinic. The mode of information delivery is paramount when providing advice of this kind, often to people newly diagnosed, who are given a large amount of information in short amount of time about huge life changes. Specific conditions also have specific barriers to uptake and adherence, e.g. in MS, cognitive symptoms that effect a person's ability to process information. Research into the best way to provide information to patients to increase uptake and adherence to is crucial to ensure that benefits are realised.

The final area of research that should be funded under secondary prevention is that of early access to treatments. Early intervention and treatment of people with chronic diseases pays dividends. This is known in MS and in other diseases. However, clinical trials of immune therapies or other treatments for people at the earliest stage of the disease, clinically isolated syndrome (CIS), before a formal diagnosis of MS, are needed to determine whether treatment of this group would prevent conversion to MS. People with CIS are already showing symptoms of MS, and damage to the brain and spinal cord has already occurred. Preventing conversion to MS by holding them at a disease stage with fewer symptoms and disability would provide better health outcomes and reduce the burden of MS on society and the health system.

If you identified a third gap in Question 8 what specific priority or initiative can address this gap? (max 500 words):
Funding needs to be provided to develop and implement national care pathways for chronic disease. In MS, the process for diagnosis, and sometimes access to diagnostic tools (such as MRIs), can be drawn out. We have data to show that in MS and many other chronic diseases, this access to early interventions can have lifelong consequences for patients, allowing them to remain productive members of society for longer. However, research is urgently needed within the Australian health system, at the level of health service delivery to determine the barriers to speedy diagnosis and early interventions, trial ways to break these down, increase communication at various levels of the health service and between health care providers and ultimately deliver the best possible outcome for Australians living with a chronic disease.

Multi-disciplinary care is one way that communication is increased and multiple levels of care can be delivered to an individual patient. In MS, coordination of care through MS clinic nurses is also of perceived benefit. Funding into research to demonstrate that multidisciplinary care for all chronic diseases and the pivotal role of MS nurses in coordinating the management of MS for individuals provides better patient outcomes and is more cost effective than standard care.

10 What Strategic Platforms (identified in the MRFF Strategy document) would the Priority/ies you identified in Question 8 fall under?

Health services and systems, Capacity and collaboration, Trials and translation

11 How can current research capacity, production and use within the health system be further strengthened through the MRFF? (max 500 words)

Please give us your views:
Research capacity and production would be strengthened through further support to embed research into the health system, through the encouragement of collaborations through clinicians, nurses, fundamental researchers and allied health researchers and professionals through the funding of national collaborative networks by area or disease or through the paired fellowship schemes described above. Both of these models break down barriers between research and clinics and ultimately deliver research outcomes to patients that are more relevant, timely and beneficial.
Research directly into the health system and care pathways, to ensure the delivery of the best multidisciplinary care, especially for chronic diseases such as MS will provide dividends in better health outcomes and cost effective treatment across the population. Research is needed to demonstrate the benefits of these strategies and provide an impetus to health systems to make much needed change, especially outside metropolitan centres.

Better use of research within the health system requires the rapid and accurate translation of research findings to the clinic. This translation step is one that has long been identified as lacking in the Australian landscape and needs to be tackled through a range of initiatives, expanding the current biomedical translation priority to include partners beyond licensed fund managers to enable pre-clinical to early clinical translation would provide further opportunities for the crucial area of translation. Another key area of translation for MS is the translation of research findings on risk factors and the factors that affect the course of a patient's

disease into interventions and management to provide secondary prevention in people at the earliest stages of their disease. This along with expanding the current funding of public good clinical trials of interventions/medications that are not of interest to commercial funders, rather than only to population groups not traditionally covering in clinical trials, will ensure that evidence-based and potentially cost-effective healthcare strategies are pursued and delivered for all Australians.

12 Do you have any additional comments on the Discussion Paper? (max 250 words)

Please give us your feedback on the Discussion Paper:
General priorities align very well with many of the goals that are currently being pursued by MS Research Australia and we feel that many of the stated objectives of the MRFF match with the objectives set out by MS Research Australia in our recent Roadmap to Defeat Multiple Sclerosis in Australia. However, MRFF requests for application seem to be much more targeted, have specific and narrow requirements, or have not completely addressed the priorities as originally set out. This, combined with the short advance notice and application times for upcoming funding opportunities means that applications may be less developed and merely support existing collaborations rather than fostering new relationships. This may ultimately lead to the funding of less innovative and transformative research. Greater transparency in the upcoming funding opportunities and longer application times will lead to higher quality science, more productive and well thought out collaborations and better value for the funding investment.

13 Do you consent to this submission being made public on the MRFF website?

Yes