MiNDAUS National MND/ALS Registry

MiNDAUS PARTNERSHIP

together into the future

MiNDAUS

Patient Registry

MiNDAUS

Clinical Registry

Framework

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The MiNDAUS Partnership

This partnership was founded in 2017 and funded by a 2018 National Health and Medical Research Council (NMRC) Partnership Grant (Kiernan, Wray et al. 2018), led by Principal Investigator Professor Matthew Kiernan (University of Sydney). A full list of partners and their affiliations is available in Appendix A.

The MiNDAUS Partnership builds on and extends existing national collaborations in a continuing effort to improve the standard and coordination of care for people with MND in Australia, and to enhance the prospects of discovering a cure or treatment. Relationships have been developed between leading clinical and research groups and patient-centred organisations, care providers and philanthropy with a shared vision.

Project Team

National Team

Assoc Prof Paul Talman, MiNDAUS Governance Committee Chairman
Catherine Hansen, Data Operations Manager, MINDAUS Registries

Site Specific Coordinating Project Staff and Participating sites

Prof. Ostoja Steve Vucic, Calvary St Joseph's, Auburn NSW,
Prof Ostoja Steve Vucic, Brain and Nerve Research Centre, Concord Hospital, NSW,
Prof. Matthew Kiernan, Brain and Mind Centre, University of Sydney, NSW
Prof. Dominic Rowe, Macquarie Neurology, Macquarie University, North Ryde, NSW
Dr David Schultz, Flinders Medical Centre, Bedford Park SA
Assoc Prof. Rob Henderson, Royal Brisbane and Women's Hospital, Herston, Qld
Dr Antony Winkel, Sunshine Coast University Hospital, Qld
Assoc Prof. Paul Talman, Barwon Health, Belmont, Vic
Dr Susan Mathers, Calvary Health Care Bethlehem, Parkdale, Vic
Prof. Merrilee Needham, Fiona Stanley Hospital, Murdoch, WA
Dr Dev Nathani, Sir Charles Gairdner Hospital/Perron Institute Nedlands, WA
Dr Lauren Giles, Launceston, Tasmania.
A detailed list of sites with contact details is maintained by the MiNDAUS Partnership and is a supporting document to this application.

Background

Australian Motor Neurone Disease Registry (AMNDR)

Since 2004, patients attending Specialist MND Clinics around Australia have had the opportunity to be enrolled in the Australian Motor Neurone Disease Registry (AMNDR) (Australian Motor Neurone Disease Registry 2020) which collects clinical and disease progression data. AMNDR

needed to be expanded and updated to a more secure platform to permit easier data entry and analysis. Currently, AMNDR holds the non-identified clinical data of 2,600 patients.

Sporadic ALS Australia Systems Genomics Consortium (SALSA-SCG)

This consortium was established in 2015 with a grant through the Motor Neurone Disease Research Institute of Australia (now known as MNDRA) established with funding received from the Ice Bucket Challenge. SALSA has been successful in establishing collaborative relationships with clinicians, researchers and patients with MND/ALS.

SALSA-SCG (2019) has achieved a world class genomics database which through a collaboration between Specialist MND Clinics and their patients from around Australia. SALSA-SCG continues this work currently due to funding sourced from the MiNDAUS Partnership and from FightMND.

The aim is to integrate the clinical data obtained from AMNDR and the biological data analyses performed by SALSA-SCG into a powerful tool for investigating the genetic and possible environmental causes of MND. SALSA-SCG also established international collaborations for data analyses and collation with Project MinE(2020). A full report of the first five years is available (Henders and Wray 2019).

MiNDAUS Patient and Clinical Registry

The MINDAUS Partnership has developed an online platform which will have two interfaces, the MiNDAUS **Patient** Registry for patient and family carer use and the MiNDAUS **Clinical** Registry which will accumulate real-time, quality-controlled clinical data relevant to patient care and research. The MiNDAUS Registry is now complete and will replace AMNDR, pilot testing will be completed at Flinders Medical Centre. The benefits of this registry are:

MiNDAUS Patient Registry

The MiNDAUS Patient Registry **will allow people with MND the choice of recording information about themselves**, their diagnosis and their specific care needs on a platform which makes it easy to complete, easy to update and easy to share with people of their choosing. The patient can decide to create a document titled 'About me and MND' with the details they have entered which can be emailed, printed, or viewed on their device. This document could be shared with a new GP, a new Allied Health Professional such as a Speech Pathologist, or a hospital or respite care service, for example.

MiNDAUS About me and MND Registry Fo

A copy of this interactive document has been inserted here:

A copy of this document-distinguished by an orange cover and called 'MiNDAUS About Me and MND General Version', will be made available to clinics and MND Associations in order to demonstrate the form.

The MiNDAUS Patient Registry **will give patients and their carers control over their information** and removes the time-consuming task of creating such documents for themselves. This platform will also allow patients to invite their carers to share, edit and update their information

and will also allow the patient to remove this access at any time. As part of the Registration process, patients will be asked if they wish to also take part in the MiNDAUS Clinical Registry.

MiNDAUS Clinical Registry

The MiNDAUS Clinical Registry **will collect relevant patient data which will allow MND Clinicians and researchers to better understand the different forms MND takes and what might cause these differences**. Clinical data relevant to MND is collected and entered by researchers during routine clinical visits. The Registry will also help us understand how safe and effective different treatments and medicines might be. Any personal information will only be collected and stored with the consent of each participant, and the information collected will only be used according to State, Federal and International laws and guidelines governing privacy.

The MiNDAUS Clinical Registry **will also provide access to research for registered participants** which includes the possibility of clinical trials. This approach is designed to improve care and treatment of MND and ensure the best outcomes possible for people living with MND. Access to data by third parties will require approval from the MiNDAUS Governance Committee and separate institutional ethics approval specific to the research being proposed.

MiNDAUS Governance

The MiNDAUS Partnership collaboratively assumes ultimate responsibility for the quality and integrity of the clinical data and overall responsibility for the conduct of the MINDAUS Patient and Clinical Registry and takes responsibility for development, management, and financing. However, the MiNDAUS Partnership delegates oversight of the use of the MiNDAUS Registries to the MiNDAUS Registries Governance Committee (MiNDAUSgov).

Sponsor

Role of Sponsor

University of Sydney is acting in the capacity of Sponsor and assumes ultimate responsibility for the quality and integrity of the clinical data and overall responsibility for the conduct of the MiNDAUS Patient and Clinical Registry and takes responsibility for initiation, management, and financing. However, University of Sydney delegates its Sponsor study-related duties to the MiNDAUS Registries Governance Committee, as set out in this document.

University of Sydney acts as the legal entity for those research activities that can only be undertaken by a legal entity. Contracts with external parties will be between the Sponsor and these parties. That is, the Sponsor delegates oversight of use of the MiNDAUS Patient and Clinical Registry to MiNDAUSgov, who will require contractual agreements that set out the roles and obligations of all involved parties.

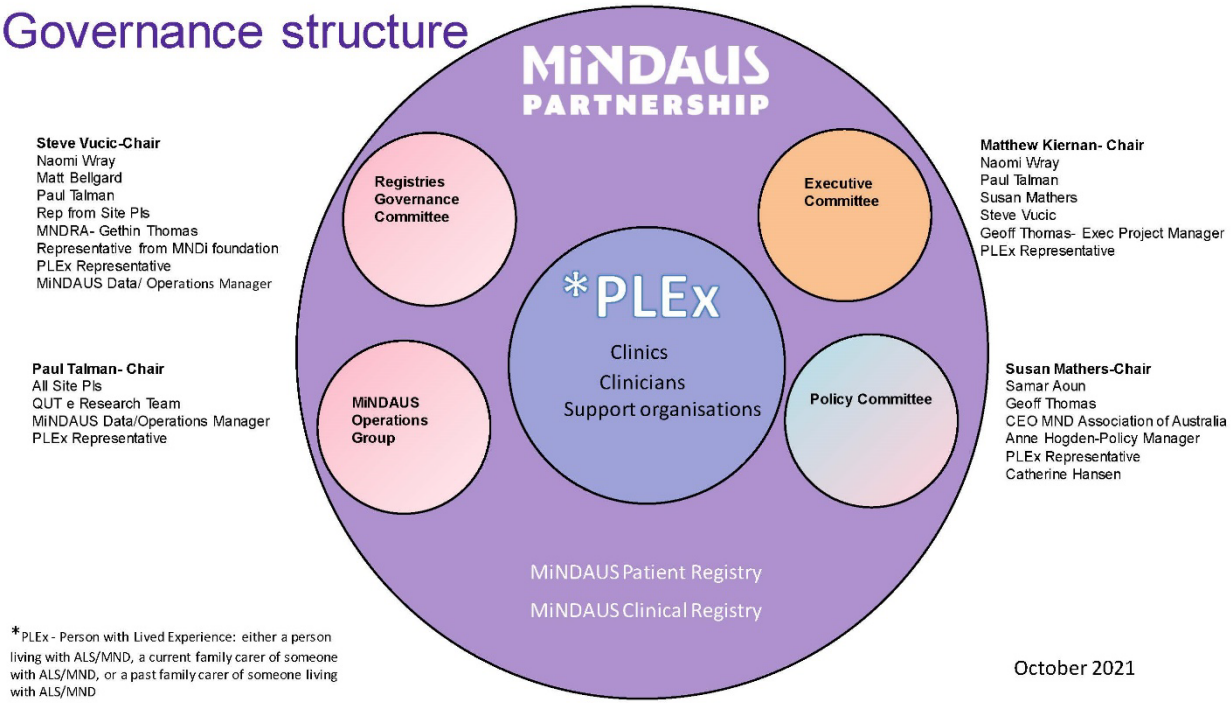
The University of Sydney will remain Sponsor until such time as the MiNDAUS Partnership formalises its own legal structure.

Insurance

The MiNDAUS Partnership has insurance through the University of Sydney in accordance with the relevant legal requirements.

Governance Framework

Figure 1:Diagrammatic representation of the MiNDAUS Governance Framework, with inaugural committee membership.



People with lived experience (PLEx) engagement

The MiNDAUS Partnership was formed with people with MND, their family carers and their families at the centre, providing the inspiration for every step taken in developing the MiNDAUS Registry.

To enable us to ensure that our initiatives reflect the aims and objectives of people with MND and their family carers, we are establishing a PLEx advisory group to ensure that every current and future committee has substantial PLEx representation. A comprehensive policy for PLEx engagement is being developed so as to maximise the influence of lived experience, based on guidance from the NHMRC (NHMRC 2018), and informed by the consumer engagement framework pioneered by Cancer Australia (Cancer Australia 2021) which has been continued by others, such as the Black Dog Institute (Suomi, Freeman et al. 2020).

Roles and Responsibilities of Committees

The roles and responsibilities of the various committees are listed below. The membership represents the committees current at the approved date of this document, with specific

acknowledgment that those with expertise in the wider Partnership, as well as in the scientific, health, research and general community external to the Partnership can be invited to participate and to become members of MiNDAUS. This reflects a dynamic structure underpinned by the processes of the MiNDAUS Constitution, currently in draft form.

MiNDAUS Partnership Group

Committee	Membership	• Roles and responsibilities
MiNDAUS Partnership Group	All founding MiNDAUS Partners	• Collaboratively agree on the aims and future directions of MINDAUS • Collaborate on publications • Identify opportunities for national and international collaboration • Identify opportunities for future funding • Actively seeking funding opportunities and grants available • Collaborating on the grant submission process • Identifying the need for new data variables • Identifying the need for new functionality to the Registries • Forming new sub committees as needed
	Replacement Organisational delegates due to partner organisations employment changes and accepted by MiNDAUSgov	
	New Partners invited by any MiNDAUS Partner and accepted by MiNDAUSgov	
	Other individuals or organisations request to become members	
	PLEx advisory group	

MiNDAUS Executive Committee (MiNDAUSexec)

Committee	Membership	• Roles and responsibilities
MiNDAUS Executive Committee (MiNDAUSexec)	Prof. Matthew Kiernan-Chair Prof. Naomi Wray Assoc. Prof. Paul Talman Prof. Steve Vucic Dr Susan Mathers Exec Project Manager, Geoff Thomas Person with lived experience (PLEx) representative	• Responsibility for the overall direction of the MiNDAUS Partnership • Responsibility for budgets • Decisions on suitability of proposed new Partners • Decisions on collaborative opportunities

MiNDAUS Registries Governance Committee (MiNDAUSgov)

Committee	Membership	• Roles and responsibilities
MiNDAUS Registries Governance Committee (MiNDAUSgov)	Prof.Steve Vucic- Chair Prof. Naomi Wray Prof. Matthew Bellgard Representative from Site PIs Representative from MNDRA Representative from MNDi Foundation	• Assess the opportunities for collaborations identified by the Partnership. • Assessing the suitability of proposed new Partners. • Delegate or form working committees as needed.

	PLEx representative MiNDAUS Data/Operations Manager Catherine Hansen	• Assess and grant or refuse the requests for data access on their merit and ethical review. • Design and implement a data access fee policy.

MiNDAUS Operations Group (MiNDAUSops)

Committee	Membership	• Roles and responsibilities
MiNDAUS Operations Group (MiNDAUSops)	Assoc. Prof Paul Talman-Chair Catherine Hansen MiNDAUS Data/Operations Manager Catherine Hansen E-Research Team- QUT Representative from site PI's PLEx Representative	• Report to MiNDAUSgov on operational matters • Refer requests for data access • Add and create new forms for data variables, implement and test • Ensure completeness and quality of data • Collate feedback and requests for new features • Consult and create carer functionality

MiNDAUS Policy Group (MiNDAUSpol)

Committee	Membership	• Roles and responsibilities
MiNDAUS Policy Group (MiNDAUSpol)	Dr Susan Mathers- Chair Project Policy Manager, Dr Anne Hogden Prof. Samar Aoun Geoff Thomas CEO MND Association of Australia PLEx Representative Catherine Hansen	• Identifying areas of need for policy change • Structuring projects to address areas of need, grant submission. • Identifying need for new data variables to inform policy direction. • Sourcing funding opportunities

Funding

This research has been partly funded by the Australian National Health and Medical Research Council (NHMRC) which has provided funding for this project for 5 years, under the 'Partnering with Consumers' Grant scheme, Application ID 1153439 2018. The funding for this type of grant relies on an equal amount of funding being obtained from the community. Our community funding has been obtained from the following sources:

- Motor Neurone Disease Research Association (the research arm of the Motor Neurone Disease Association of Australia)
- Australian Motor Neurone Disease Registry
- Motor Neurone Disease Association of Western Australia
- Thomas MND Research Group
- Motor Neurone Disease Association of Australia
- MND and Me Foundation

In addition, MiNDAUS benefits from work that was started from funding from other sources. In particular:

- Foundation for Angelman Syndrome Therapeutics
- Racing for MNDi Foundation
- FightMND
- The Ice Bucket Challenge
- MTP Connect

Ongoing funding sources are still being pursued to secure continuance of the MiNDAUS Registries into the future.

The costs of providing data access to third parties will be recovered and this process will be managed by the MiNDAUS Registries Governance Committee.

Project Description

Significance

Motor neurone diseases (MND) are adult-onset neurodegenerative disorders where progressive motor weakness leads to death, usually from respiratory failure. In Australia, an estimated 2000 people are living with MND at any given time (Deloitte Access Economics 2015). While some people can live a long time after diagnosis, the majority survive only 2 to 3 years. The rapid morbidity of the disease puts our health system under particular strain and care is often provided by informal or family carers (Aoun, Birks et al. 2020).

Research into treatments and potential cures is hampered by economics, the relatively low prevalence of the disease and the rate of progression. However, patients consistently identify a desire to participate in the quest for a cure (Halpin, Savulescu et al. 2015, Mathers and Talman 2017), and around the world there are many patient and family led philanthropic organisations willing to fund clinical trials where governments and Pharmaceutical companies hesitate (MND and Me Foundation Ltd 2016, Fight MND 2020, I am ALS 2020, Les Turner ALS Association 2020), among others. Charitable advocacy organisations such as the research arm of the Motor Neurone Disease of Australia (MNDA), Motor Neurone Research Australia (MNDRA), are also active in this space. There is only one approved treatment shown to extend life expectancy which is a drug called Riluzole, which may extend life by three to five months (Dharmadasa and Kiernan 2018).

Supportive treatments are the mainstay of care, such as breathing, nutrition, mobility and communication support, in addition to complex symptom management (National Institute for Health and Care Excellence (NICE) 2016). Loss of functional speech occurs in the vast majority of people with MND (Bongioanni 2012, Elliott, Newton et al. 2020), and a spectrum of cognitive and behavioural impairment occurs in around 50% of all people with MND (Hsieh, Caga et al. 2016). These two factors increase the need for specialist referral and support for both the patient and the family carer (Burke, Hardiman et al. 2018, Elliott, Newton et al. 2020).

Evidence promotes the role of team-based, multidisciplinary care for people with MND to provide multidimensional assessment, symptom management and care-planning (Dharmadasa 2016, National Institute for Health and Care Excellence (NICE) 2016). In Australia, Specialist

Multidisciplinary Clinics operate in major population centres. Factors such as the distance a patient may live from one of these clinics, and the often rapidly increasing disability of the person with MND mean that the care provided by a Specialist Clinic needs to be supplemented by regional and community health services and organisations, such as State-based MND Associations (Aoun, Birks et al. 2020), which differ in the amount and type of support they offer. At best they offer specialised equipment loan services, home visit programs and support groups for people living and dying with MND, their family carers and their families.

A further complicating factor in the delivery of coordinated services is the inequity in funding between those who are eligible for the NDIS (under 65 years old) and those who need to access the Federal Government's My Aged Care system (Hogden, Paynter et al. 2020).

The assimilation of the clinics in major centres with other health and community service providers to meet each person's needs and preferences is currently more ambition than reality, partly because there may be up to 22 separate Health Care Providers involved in the care of one person with MND (Mathers and Talman 2017).The fragmentation of care is illustrated by the following quotes from bereaved carers in WA (Aoun 2020)):

> *Our care was chaotic. No one knew who was doing what, no co-ordination. It was in the roll out and trials of NDIS in WA and really cannot sum up how poor it was. Much of my time was spent trying to wrangle specialists and appointments whilst trying to deal with caring for my husband in the face of his terminal illness diagnosis. We both were in shock and had not really faced any reality of his diagnosis when he suffered respiratory failure in our home in the middle of the night, just days after an appointment with a respiratory specialist and only 3 months after his eventual diagnosis with MND. 3 months of stress and trauma trying to get the right care and support services in place instead of any worthwhile time together. The process not his illness exhausted us both and I believe took him before time.*

> *Our experience has been heartbreaking and we are still in the midst of it. My dad is being moved from hospital to hospital and finding palliative care is impossible. The system is broken and needs to be fixed. MND is a diagnosis that needs its own system to help understand the impact.*

In summary, there remains a significant challenge of cohesion, with a need across diverse organisations to develop cogent, coordinated policies that recognise the potential of duplication and inefficiencies between the competing priorities of drug discovery, clinical trials, service delivery and research funding.

Aims and Objectives.

The aims of the project are to implement the MiNDAUS Patient Registry and the MiNDAUS Clinical Registry.

The objectives of implementing the registries are expressed according to the four ethical principles.

Supporting the ethical principle of Beneficence

The MiNDAUS Partnership will invite patients and carers to join the MiNDAUS Patient Registry, which will:

a) Empower patients and carers to:

i. enter, control, and share their details to enable better patient-centered care, communication and coordination of care across health services and organisations
ii. improve self -management.
iii. access quality information
iv. access and explore research opportunities of which they might otherwise remain unaware.
v. access Specialist Multidisciplinary Clinic services and expertise, even as a remote patient
vi. contribute to the Genomics project, SALSA-SCG.
vii. empower patients and their carers to ask to participate in the MiNDAUS Clinical Registry.

The MiNDAUS Partnership will invite participation in the MiNDAUS Clinical Registry, which will:

b) Integrate established national data capture systems to improve efficiency and validity of the data, and:

i. allow analysis of the historical dataset as well as the newly collected dataset.
ii. ensure the clinical data is future proofed so as to allow linkage to eHealth Records and PBS data subject to stringent security protocols.
iii. enable data sharing between healthcare professionals, thus enhancing communication between different healthcare service providers.
iv. allow analysis of disease progression measures.
v. allow clarification of the different types of MND so that existing and potential treatments may be better tailored to the individual
vi. provide a resource of suitable patients for future observational and clinical trials
vii. allow analysis of incidence, environmental factors, service provision and use in order to inform future policy directions nationwide.
viii. unify and integrate the digital platforms to make Australia more attractive to national and international biotechnology companies for early phase clinical development of MND treatments.

Supporting the ethical principle of Autonomy

c) Participants will have the power to decide:

i. whether to participate in the Patient Registry and to control which information they need and wish to enter.
ii. to withdraw from participation at any time.
iii. to allow their carer to access and edit their information.
iv. to revoke the permission for carer access at any time.
v. to upload and share their legal documents about future care, such as Advance Care Plans.
vi. to share their information with a new healthcare provider.
vii. whether to participate in the MiNDAUS Clinical Registry.
viii. whether to allow themselves to be invited to participate in future research, and to consent to take part or to withhold their consent.
ix. to withdraw their permission at any time for participation in the MiNDAUS Clinical Registry.

Supporting the ethical principle of Justice

d) Inclusion of all people diagnosed with ALS/MND.

i. The inclusion of all people diagnosed with ALS/MND across Australia irrespective of the type of MND they are diagnosed with, their rate of progression, time since diagnosis and geographical location.

e) Real time information on service delivery, quality and access:

i. will inform new national policies for best practice service provision which will address the issues of poor coordination of care across multiple services and providers.
ii. will address the inequities of care across jurisdictions by informing the development of evidence-based guidelines and policy initiatives.
iii. will allow benchmarking across services nationwide to ensure there is less geographical disadvantage for patients and carers.

Supporting the ethical principle of non-maleficence

As this is an observational study and no intervention is being trialed, the main risk to participants is unauthorized access to their data.

f) In order to protect participant privacy:

i. The MiNDAUS Partnership has developed a comprehensive Data Management Policy and the full document is available as a supporting document to this Framework.
ii. Data will only be shared with third parties under the strict policies set out in the MiNDAUS Data Management Policy, and where access has been permitted under those rules by MiNDAUS Registries Governance Committee and mediated by the MiNDAUS Data Operations Manager. MiNDAUS has developed Standard Operating Procedures on data access and sharing.
iii. Project staff will receive appropriate training as necessary about patient confidentiality as part of the site induction process. It should be noted that in most cases, the project staff are the same personnel already working as project staff for AMNDR and SALSA-SCG and have already demonstrated their understanding and ethical approach to patient confidentiality.

g) Participants continuing treatments and engaging in clinical trials

iv. As this is an observational study, no intervention is being trialled and so participants are free to pursue treatments as recommended by their health care providers.

v. Participants are not prevented from participation in clinical trials or other research that they decide to take part in.

Project design and methods

Study procedures

a) Recruitment and gaining Informed Consent from participants

With respect to the frequency of communication difficulties experienced by people with ALS/MND, consent will be considered valid if it is given via whatever method the person with MND normally employs. This will include an electronic consent on the Registry website; a 'verbal' consent from a text to speech program on an electronic device; a written signature; a verbal consent, or consent from their Legal Representative.

i. Patient self-register pathway

Information about the MiNDAUS Patient and Clinical Registries will be available on the Motor Neurone Disease Australia website with a link to the MiNDAUS website.

Any person diagnosed with MND in Australia is eligible to register themselves for the MiNDAUS Patient Registry, and consent will be obtained by a carefully controlled consent process via a Patient-Web Interface. During this process, the patient will have the opportunity to also register to participate in the MiNDAUS Clinical Registry, and nominate the Specialist MND Clinic which they attend, or will attend. During the next clinic visit, the project staff will be able to view the electronic consent, offer any further information necessary, and answer any questions the patient or their carer may have.

ii. Clinic visit pathway

All patients presenting to a clinical site for a scheduled visit will be given information about the MiNDAUS Patient and Clinical Registries. Wherever possible, the participant information sheet and consent form (PICF) for the MINDAUS Clinical Registry will be sent to the patient prior to their appointment or provided at first registration prior to seeing their doctor.

Individuals will then be approached by the Coordinating project staff, or their representative and will be asked to participate.

- Existing clinic patients will often already be participating in the Australian Motor Neurone Disease Registry (AMNDR). If so, an explanation will be provided about the integration of AMNDR into the MiNDAUS Registries and the advantages and potential disadvantages of continuing their participation. Consent to participate will include permission to link their AMNDR ID to the MiNDAUS Registry.
- An explanation will be provided to new clinic patients about the advantages and potential disadvantages of participating in the MiNDAUS Registries and their consent to participate will be sought.
- A blank copy of the 'About Me and MND' form (MiNDAUS About Me and MND General Version) will be available to demonstrate the utility and possible benefits to participation in the Patient Registry.

iii. *Project staff training*

Project staff obtaining the consent will receive training to ensure that they are aware of their responsibilities, are capable of answering all questions and are sensitive to the needs of the patients and any possible issues that may arise. Project staff, aside from the PI at each site, will be, in most cases, employed for activities surrounding research and will not necessarily be part of the patient's usual clinical team. This arrangement avoids patients feeling obligated to participate by virtue of a dependent relationship with a clinician. In any case, project staff will receive training to ensure that any potential pre-existing relationship does not unduly influence participation. Patients will be encouraged to discuss their participation with someone in whom they trust and it will be made clear to them that their relationships with their clinicians and healthcare team will be unaffected by their decision.

Training will be consistent with the principles outlined in the ICH guideline for Good Clinical Practice (Therapeutic Goods Administration 2016), Declaration of Helsinki(World Medical Association 2013) and the National Statement on Ethical Conduct in Human Research (NHMRC, Australian Research Council et al. 2007).

iv. *Need for an Interpreter*

An ability to 'speak' either verbally, electronically or in a written form and understand English is required but we will provide interpreter services wherever possible and a proxy/translator will indicate that they believe the person has understood the content sufficiently to make a free and valid decision.

v. *Consent process*

Prospective participants will be given sufficient time to read the information and to discuss any concerns they have prior to giving consent. It is important to note that they do not have to give their consent at the first appointment if they do not wish to. Clear information will be given that consent is voluntary, that if they don't it will not affect their care in any way and that they are free to withdraw at any time, noting the consideration that if their samples and data have already been used then that cannot be rescinded. A hard copy or electronic copy of the signed informed consent will be given to the participant. If completed in hard copy, the original signed form will be scanned and uploaded to the Registry.

The MiNDAUS Partnership has developed a Standard Operating Procedure for obtaining Informed Consent. (SOP-MG-01) which is a supporting document to this Framework.

vi. *Confirming consent*

At each clinic visit, participant consent for participation in the MiNDAUS Clinical Registry will be verbally reconfirmed by the Coordinating project staff or their representative prior to commencing data collection.

The participant's consent for participating in the MiNDAUS Patient Registry is implied by their continuing use of the Registry.

vii. *Terms of the consent*

Extended and unspecified consent will be sought according to the National Statement on Ethical Conduct in Human Research 2007 (updated 2018) (NHMRC, Australian Research Council et al. 2018) to;

- Hold self-report (SR) demographic data (self and family information), disease information and disease progression information as part of the Patient Registry.
- Undertake data collection and storage of clinical data collected during routine clinical visits in the MiNDAUS framework as part of the Clinical registry.

- Sharing of de-identified self-report data and clinical data between MiNDAUS partners.
- Share de-identified patient self-report data and clinical data with potential sponsors of clinical trials for the purposes of inclusion.
- Share de-identified patient self-report data and clinical data to health and support agencies to understand incidence and unmet needs.
- Share data collected / stored and on-share datasets for the purposes of progressing new research aims and for replication / validation other research projects with appropriate ethical approval. This may include the sharing of data outside Australia subject to Australian regulations.
- Store clinical and self-reported data in perpetuity so that access to data may be granted to future projects.

b) Data to be collected

For a full list of data variables for both the MiNDAUS Patient Registry and the MiNDAUS Clinical Registry, please see the supporting document: MiNDAUS Registry Data Collection Variables.
Data on the MiNDAUS Patient Registry is patient driven. Patients, or their nominated caregiver, sign-up and enter data via a series of registry modules, covering the following demographic, health and medical, equipment and service utilization. Self-report data will include the following modules:

- Module 0: Demographics
- Module 1: Consents
- Module 2: My Legal Documents
- Module 3: My Recent Symptoms
- Module 4: My Journey
- Module 5: My Needs
- Module 6: My Calculators
- Module 7: My Care Team
- Module 9: My Appointments

The demographics and consent modules are mandatory and all subsequent modules are optional.
Participants in the MiNDAUS Patient Registry will be able to create a printable, shareable form from the data entered if they wish. It is foreseen that patients may use the form as a method of introducing themselves to a new healthcare provider, paid carer or in the circumstances of an admission to a health facility. A copy of this form, called 'About me and MND' can be found as a Supporting Document to this application.

Clinical data will pertain to the following sets of information:

1. Onset of disease
2. Family History
3. Medical History
4. Tests use to provide diagnosis.
5. Regions of the body affected by disease.
6. A functional rating scale – ALSFRS-R
7. Treatments
8. Service use
9. General questions about lifestyle such as smoking status and occupation.

c) Participant withdrawal

Study participants may be discontinued from the MINDAUS Clinical Registry entirely according to predefined criteria for discontinuation. Additionally, a participant may be discontinued from a trial or substudy but remain in the MINDAUS Clinical Registry.

Criteria for discontinuation from the MINDAUS Clinical Registry entirely include:

viii. The treating clinician considers continued participation is not in the best interests of the participant.

ix. The participant or their Legal Representative requests withdrawal from ongoing participation.

In the case of discontinuation, the reason(s) for withdrawal will be documented. Following discontinuation, participants will be treated according to an appropriate standard of care by their treating clinician.

d) Data collection techniques

In all possible cases, the data collected during the normal clinic visit, will be used to complete the data requirements for the MiNDAUS Clinical Registry, to avoid overly prolonging the time the patient needs to spend in clinic.

Data entry and data management will be coordinated by the MiNDAUS Data Operations Manager, and the Coordinating Principal Investigator, Assoc. Prof Paul Talman, including accessing programming and data management support.

Site procedures to ensure data quality and protocol adherence include:

- Start-up meetings for all site coordinators and investigators will be held prior to study commencement to ensure consistency in procedures.
- Regular meetings will be held between all site project staff and the MiNDAUS Data Operations Manager.
- A paper-based Case Report Form will be made available to all sites for reference, and as a backup strategy in the case of an inability to connect to the internet. Site staff will enter the data thus collected into the MiNDAUS Clinical Registry at their earliest convenience and organise the secure destruction of the paper document.
- Site induction will occur for each participating site before study initiation. This will include training of clinical staff and development and dissemination of Standard Operating Procedures.
- A detailed dictionary will define the data to be collected on the MiNDAUS Clinical Registry with the incorporation of data validation and prompts where appropriate.
- The data management centre will perform timely validation of data, queries and corrections if errors are found during quality control checks.

All project personnel will understand the importance for data security in accordance with NHMRC guidelines.(NHMRC, Australian Research Council et al. 2019)

e) Enabling the collection of clinical data for people with MND who do not attend a participating clinic

Members of our PLEx Advisory Group asked us to design a process by which people with MND who do not attend a participating clinic could contribute their clinical data. It was the opinion of these PLEx Advisors that otherwise, people with MND outside of a participating clinic would

neither have the advantage of being stratified for potential research projects based on clinical parameters nor transparency over their clinical information and the ability to control and share it. Accordingly, we have made it possible, and optional, for a patient to download a relevant Case Report Form, eg, First Visit or Subsequent Visit, from the Registry and take it to their Specialist for completion. This form includes sections that can be completed by a Patient and/or their Carer on their behalf. Once the form is completed, the Patient saves it as a pdf and uploads it to the Registry. The Patient is asked to provide an email address for a person, such as their next of kin, who is prepared to be contacted once there has been no activity on the Registry for 12 months.

1. *Follow up and missing data*

Project personnel will perform regular and timely validation of data, queries and corrections. Any common patterns of errors found during quality control checks will be fed back to participating sites. Missing data will be minimized through a clear and comprehensive data dictionary with online data entry including logic checks.

2. *Co-enrolment with other trials*

Co-enrolment of participants in other studies, including interventional and therapeutic trials, is allowed. The principle is that co-enrolment should always be allowed except when there is a clear threat to the validity of either study, or it would materially influence the risk to participants. Decisions regarding co-enrolment with other trials will be made on a trial-by-trial basis. The decision regarding co-enrolment will lie with the MiNDAUS Registries Governance Committee. Decisions regarding co-enrolment with other trials will be distributed to participating sites as an operational document and will not require or involve amendment of this protocol.

3. *Cooperation between the MINDAUS Clinical Registry and other trials with overlapping populations or interventions*

During the lifetime of the resource there will be other studies that will have inclusion and exclusion criteria which include participants who are eligible for the MINDAUS Clinical Registry. The MINDAUS Partnership seeks to cooperate and coordinate maximally with other studies in accordance with NHMRC guidelines (NHMRC 2018). Examples of such cooperation and coordination would include, but not be limited to, utilisation of MiNDAUS Clinical Registry infrastructure for screening and enrolment to other studies and sharing of data and biospecimens collected. In this case, access to the data would be granted by the MiNDAUS Registries Governance Committee and mediated by the MiNDAUS Data Operations Manager acting as data custodian.

4. *Linkage to external data set held by the Sporadic ALS Australia Systems Genomics Consortium (SALSA-SCG)*

The MiNDAUS Clinical Registry will link to the (SALSA-SCG) dataset and this linkage will be consented to specifically by the patient at registration or enrolment.

5. *Linkage to other external datasets*

The MiNDAUS Clinical Registry may seek to access external resources such as personal information held by other parties to enrich the core data sets, eg GP records or data from the Medicare Benefits Schedule (MBS) and the Pharmaceutical Benefits Scheme (PBS). The consent

requested anticipates this and any data brought in from external resources will be managed under the spirit of the consent outlined for the MINDAUS Clinical Registry. That is, data will be managed in such a way that a participant's privacy and confidentiality will be maintained at all times. It will be likely that bringing in such data will be governed by external ethical review such as is provided by the AIHW for access to federal health information.

f) Data Management Policy

The MiNDAUS Patient and Clinical Registries have been developed and created using the Trial Ready Registry Format (TRRF), under the supervision of Professor Matthew Bellgard at Queensland University of Technology.

TRRF is a modern, highly secure framework with a fully configurable permissions layer. The framework offers state of the art security features incorporated in every aspect from the programming language used, the design of the software, the security of access, and the way it is stored. In order to provide the highest level of privacy protection, all traffic to and from the platform is encrypted, and any identifying data is kept in a separate area to clinical or self-reported data.

The MiNDAUS Patient and Clinical Registries will be hosted on Amazon Web Services (AWS) Australian based servers and will be protected by AWS advanced security measures in addition to the securities inherent in the software itself and the security policies adopted by the MiNDAUS Partnership.

AWS is a trusted provider of hosting services by the Australian Federal Government (Australian Cyber Security Centre 2019)

Supporting documents

This Framework document is supported by the following documents:

MiNDAUS Registry Data Collection Variables V 1.1

MiNDAUS Privacy Policy V1.0

MiNDAUS Clinical Registry paper based CRF V 1.3

MiNDAUS About me and MND Registry Form V 2.0

MiNDAUS About Me and MND General Form V 1.1

MiNDAUS Standard Operating Procedure Informed Consent V 1.0

MiNDAUS Clinical Sites Details V 1.0

MiNDAUS Clinical Registry national PICF Template V 1.2

Appendix A

MiNDAUS founding partners

Professor Matthew Kiernan, Brain and Mind Centre, University of Sydney
Professor Naomi Wray, Queensland Brain Institute, University of Queensland
Assoc Professor Paul Talman, Barwon Health Victoria; Monash University, Melbourne
Professor Steve Vucic, Westmead Hospital, Sydney
Dr Susan Mathers, Calvary Health Care Bethlehem; Monash University, Melbourne
Assoc Professor Robert Henderson, Royal Brisbane and Women's Hospital; University of Queensland
Professor Matthew Bellgard, Queensland University of Technology
Professor Samar Aoun, Latrobe University, Victoria; Perron Institute, Western Australia.
Professor Julian Savulescu, University of Oxford; Murdoch Children's Research Institute; University of Melbourne
Professor Dominic Rowe, Macquarie University; Macquarie University Hospital
Carol Birks, MND Association of Australia
Gethin Thomas, MND Research Australia
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Professor Ian Blair, Macquarie University, NSW
Geoff Thomas OAM, Thomas MND Research Group, South Australia
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Dr Anne Hogden, University of Tasmania
Professor Merrilee Needham, Fiona Stanley Hospital, Murdoch University; Notre Dame University Western Australia
Assoc Professor David Schultz, Flinders Medical Centre, South Australia
Dr Tina Soulis, Neuroscience Trials Australia
Sr Margie Zoing, Brain and Mind Centre, University of Sydney
Jane Milne, MND and Me Foundation, Queensland

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Version Control

Document History	
Version	Summary of changes
1.0	N/A First issue
1.1	Addition of new sites and personnel Insertion of updated Governance Framework diagram and personnel in Committees Removal of Appendix B Insertion of version control table Insertion of new footer table with version information
1.2	Addition of the process for collection of clinical data for people with MND who do not attend a participating clinic.