

**AMNDR Steering Committee:**

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www.amndr.org

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**OBJECTIVES**

AMNDR is a nationwide program to characterize and evaluate patients presenting with MND. Such an undertaking may help to describe clinical and demographic characteristics at presentation and throughout various stages of the disease. This initiative will provide a detailed outline of MND treatment management and associated outcomes. In addition, collecting information at a national level will provide a sample size large enough to confidently evaluate the impact of new treatment(s) and diagnostic strategies in “real life”.

The Australian MND Registry (AMNDR) will provide a means to facilitate the collection and analysis of MND patient data such as demographics, site of onset, diagnosis data, treatment type, changes in functional capacity, complications related to disease progression and the impact of new treatments and interventions for MND. An important aspect of the registry is to improve patient care through continuous evaluation of patient management and associated outcomes. This will provide Australian clinicians with an opportunity to identify treatment gaps and compare management strategies with associated outcomes at a national level. The registry will be available as a resource for researchers to test novel hypotheses and assist in enrolling patients in further research into motor neurone disease.

**METHODS**

**STUDY DESIGN**

The registry is a collaborative program involving Patients, The Australian Motor Neuron Disease Association and Australian Clinicians. It is managed via a steering committee of relevant stakeholders. Clinicians are able to register their practice site and enrol patients with MND/ALS. Patient information is collected at registration and subsequent follow-up reviews. Case Selection: Consecutive patients attending MND clinics or consulting rooms, that have been diagnosed with MND will be invited to participate in this registry. The patient or their legal authorised representative (LAR) must provide consent for data collection. Sample Size: It is estimated that in Australia, there are 1200 patients living with a diagnosis of MND at any given time. It is envisaged that this study would capture at least 80% (960) of these patients. There are approximately 370 new diagnoses per year. It is envisaged that the registry will capture at least 80% (296) of these patients per year.

Patient visit schedule and recorded information on case report forms (CRF):

**Registration** – Registration CRF to be completed

**Visit 1** - (three months from Registration Visit). Assessment CRF to be completed.

**Visit 2** – (three months from last visit). Assessment CRF to be completed.

**Visit 3 onwards** – (i.e.: Visits 3, 4, 5, etc...) to be scheduled every six months Assessment CRF to be completed.

**Completion** - If the patient dies, withdraws consent, has an alternative diagnosis confirmed or is lost to follow up for any reason, the Completion Visit CRF should be completed. Information collected at Registration and follow-up reviews relates to clinical history of disease and its progression, current clinical signs, medications, respiratory function, body weight, clinical interventions and health service utilisation. A copy of the Registration, Assessment and Completion CRF's is located on the AMNDR web site at, www.amndr.org.au Data Quality: There is a minimum 10% monitoring of cases by Quintiles HRS to ensure data quality and integrity is maintained.

**RESULTS**

292 patients were enrolled in AMNDR between August 2004 and September 2005. All states apart from Tasmania registered patients, with 88 % of registrations coming from 10 major sites (Figure 2). As of September 2005, 90 patients had at least one further follow up assessment (Figure 3).

Distinct phenotypes were identifiable using the clinical information collected in the registration data (Figure 4). In the Global MND phenotype there are combined upper and lower motor neuron signs in at least 2 regions and as a group they have the shortest survival (Table 1 and 2).

At registration 110 patients were defined as global with a mean survival of 20 to 30 months depending on the region of onset. In the Global bulbar onset group there was a predominance of females with a ratio of 25 to 17.

Flail arm and leg phenotypes were also identifiable in that they presented with lower motor neuron signs and absent reflexes in the arms and legs respectively. In the Flail Arm phenotype 15 patients were identified with a mean survival of 95 months (Table 2). The gender ratio was 14 male to a single female.

Primary lateral sclerosis (PLS) could also be readily identified in that they had upper motor neuron signs in all regions, bulbar, cervical and lumbar. All 17 patients identified with PLS were surviving at the time of analysis with a mean time of 103 months and an equal gender ratio of 8 female to 9 males.

Of the 292 registered patients 194 had been prescribed Riluzole (66%) and 15 had ceased taking the drug.

In Australia Riluzole was authorised for use in MND as of August of 2003. From the registry 101 patients had their symptom onset after this time and 73 were taking Riluzole (72%). Of the 28 patients not prescribed Riluzole 8 were over 75 years of age.

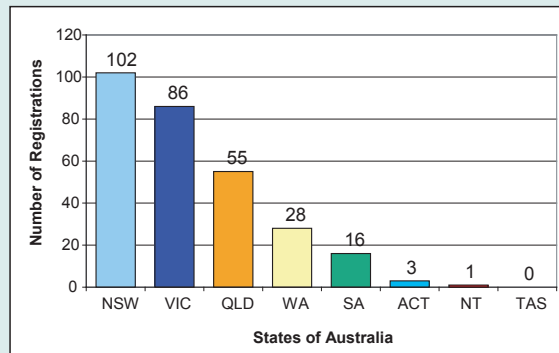


FIGURE 1: Registration by State (August 2004 - September 2005)

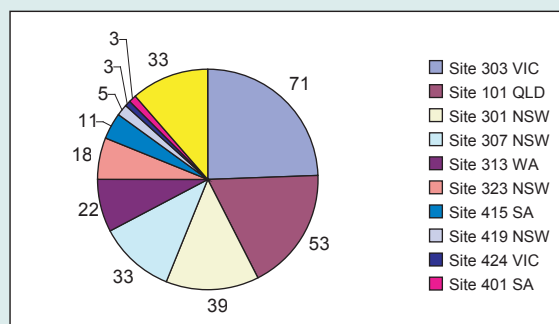


FIGURE 2: Number of Registrations - According to Sites Across Australia

**CONCLUSION**

A national registry for motor neuron disease may be an effective method for defining clinical subtypes and providing real life outcome information to Patients, Care Providers and Clinicians. It has the potential to facilitate research and benchmark standards of care.

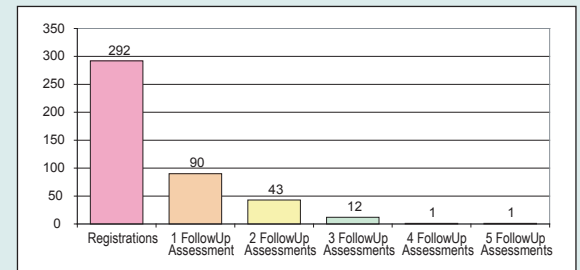


FIGURE 3: Registration and Follow-Up Assessments - September 2005

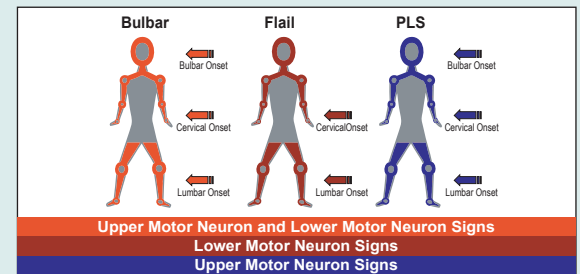


FIGURE 4: Clinical Subtypes identifiable in the data registry

	Upper Motor Neuron Signs (UMN)	Lower Motor Neuron Signs (LMN)
<b>Bulbar</b>	Jaw Jerk Positive Palatal Spasticity Tongue Spasticity	Facial Fasciculations Tongue Wasting Palatal Weakness and Fasciculations
<b>Cervical</b>	Increased tone Hyper-reflexia Preserved reflexes in wasted muscles	Fasciculations and Weakness Muscle Wasting Absent Reflexes
<b>Lumbar</b>	Increase tone and or extensor plantaris Hyper-reflexia Preserved reflexes in wasted muscles	Fasciculations and Weakness Muscle Wasting Absent Reflexes

Table 1: Clinical signs used to determine upper and lower motor neuron signs for clinical phenotyping of the patient population.

Phenotype	Region of Symptom Onset	Number of Registrations	Age at Onset Mean (St Dev) Years	Sex Ratio F:M	Deaths	Survival Months Mean (St Dev) Range
Global	Bulbar	42	64 (13)	25:17	10	27 (10) 20-48
	Cervical	39	55 (19)	11:28	5	20 (10) 7-33
	Lumbar	29	61 (10)	15:14	7	36 (16) 14-63
Flail	Arm	15	63 (13)	14:1	4	95 (85) 30-238
	Leg	15	58 (10)	10:5	1	#59 (28) 33-100
PLS	All regions	17	54 (9)	8:9	0	*103 (55) 24-259

Table 2: Clinical phenotypes identifiable in the data registry with the number of Registrations fitting each phenotype. Survival is Calculated from the data of deceased patients. While in the Flail Leg # and PLS\* phenotypes the mean, St dev and range is from all surviving patients.