



Abstracts from Themes WP and CP

Biomedical and clinical work in progress

Care practice

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Biomedical and clinical work in progress

WP-01 Prevalence of Amyotrophic Lateral Sclerosis (ALS) in the United States, 2016

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Keywords: epidemiology, disease burden, prevalence

Background: In October 2010, the federal Agency for Toxic Substances and Disease Registry (ATSDR) launched the congressionally-mandated National ALS Registry to collect and analyze data regarding persons with ALS (PALS) in the United States. ALS, also known as Lou Gehrig's disease, is a progressive neuromuscular disease that usually leads to death within 2–5 years of diagnosis. The initial symptoms of ALS vary and may include muscle weakness in upper or lower extremities, along with difficulty speaking, walking, and fatigue and eventual death. The main goals of the Registry are to determine the incidence and prevalence of ALS within the United States, characterize the demographics of those living with ALS, and identify the potential risk factors for the disease.

Objectives: Summarize the prevalence of persons with ALS in the United States for calendar year 2016.

Methods: As ALS is not a reportable disease in the United States, the National ALS Registry uses a two-pronged approach to help identify all cases of ALS in the country. The first approach utilizes existing national administrative databases (Medicare, Medicaid, Veterans Health Administration (VHA) and Veterans Benefits

Administration (VBA)) to identify prevalent cases. The second method uses a secure web portal to identify cases not included in the national administrative databases. PALS who register via the web portal have the opportunity to complete surveys that may lead to a better understanding of the potential risk factors for ALS (eg, genetics, environmental and occupational influences).

Results: Findings from the National ALS Registry's 2016 prevalence estimates will be presented at the ALS/MND International Symposium in Perth, Australia, 2019. Descriptive statistics on the prevalence rates of ALS in the US, along with demographics of cases will also be presented.

Discussion and conclusions: This report summarizes the prevalence of ALS for calendar year 2016. This is a continuing effort to identify ALS cases on a national population basis in the United States. The preliminary surveillance results capture ALS prevalence but do not reflect all incident cases since the ALS diagnosis date was not captured via the national administrative data sets. The establishment of the National ALS Registry has allowed for the analysis of prevalence of this disease as well as assess potential risk factors that may cause ALS.

WP-02 Utilizing capture-recapture methodology to estimate the missing ALS prevalent cases in the United States, 2016

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Background: In October 2010, the federal Agency for Toxic Substances and Disease Registry (ATSDR) launched the congressionally-mandated National ALS Registry to collect and analyze data regarding persons with ALS (PALS) in the United States. ALS, also known as Lou Gehrig's disease, is a progressive neuromuscular disease that usually leads to death within 2–5 years of diagnosis. The initial symptoms of ALS vary and may include muscle weakness in upper or lower extremities, along with difficulty speaking, walking, and fatigue and eventual death. The main goals of the Registry are to determine the incidence and prevalence of ALS within the United States, characterize the demographics of those living with ALS, and identify the potential risk factors for the disease.

Objectives: Estimate the percentage of missing ALS prevalent cases.

Methods: As ALS is not a reportable disease in the United States, the National ALS Registry uses a two-pronged approach to help identify all cases of ALS in the country. The first approach utilizes existing national administrative databases (Medicare, Medicaid, Veterans Health Administration (VHA) and Veterans Benefits Administration (VBA)) to identify prevalent cases. The second method uses a secure web portal to identify cases not included in the national administrative databases. Using this method nets about 80-85% of ALS cases in the U.S. Patients who get their care from private health insurance providers are not included in the above mentioned databases. Therefore, by utilizing capture-recapture methodology which is a statistical method that examines the overlap in identification of cases from different data sources such as those mentioned above and using this overlap to estimate a missing percentage of prevalent cases. This percentage will be applied to actual prevalent cases to estimate a new prevalence rate and case counts.

Results: Findings from the National ALS Registry's 2016 prevalence estimates using capture-recapture methodology will be presented at the ALS/MND International Symposium in Perth, Australia, 2019. These findings will include a new national prevalence estimate based upon the estimated number of missing ALS cases in the United States.

Discussion and conclusions: This report summarizes the prevalence of ALS for calendar year 2016 using capture-recapture methodology. This new estimate will allow the National ALS Registry to quantify ALS prevalence to include those who seek care outside traditional health delivery platforms mentioned above. This is a continuing effort to identify ALS cases on a national population basis in the United States.

WP-03 Critical epochs of environmental exposures and gene-environment-time interactions in ALS

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Keywords: gene-environment interaction, risk factor, critical exposure-times

Background: The syndrome of ALS is believed to result from exposures at critical

times and from gene-environment interactions (1). Studies of the Guam ALS “epidemic” (2-5) and in Finland (6, 7) provide some insight into the time question.

Objectives: We will determine critical epochs of exposures to many environmental risk factors for ALS, using case-control analyses of years of exposure to many ALS environmental risk factors in large cohorts of patients and controls. We will explore gene-environment-time interactions using DNA sequencing and machine learning.

Methods: We have databases of 30-years of exposures to ALS environmental risk factors “the exposomes” of >1200 ALS patients and >1200 control subjects from Piedmont (Italy), Northern New England and Ohio. We have databases of DNA sequencing “the genomes” of >1000 ALS patients and >1000 controls. We apply Multifactor Dimensionality Reduction methodologies to identify ALS gene-environment interactions.

Results: This project, supported by funding from the CDC National ALS Registry, began in October 2018. We will present the interim results of this 3-year project.

Discussion and conclusions: This project addresses the two critical issues facing attempts to understand the causes of ALS: What is the critical time-period of exposure to environmental risk factors? What part do genetic factors and environmental factors play in causation? We already have the large databases needed to address these questions. We have started to apply machine learning methodologies to these issues.

Acknowledgements: This project is funded by a grant from the National ALS Registry of the Centers for Disease Control and Prevention (R01TS000288)

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WP-04 MND phenotypes and premorbid status in the Trøndelag region, Norway

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Keywords: epidemiology

Background: Trøndelag is a region in the middle of Norway, served by two public neurological wards and outpatient clinics, located in the northern (Namsos hospital) and southern (Trondheim university hospital) area. Norway has universal health care, thus all patients diagnosed with MND will have their diagnosis from these two centres.

The Nord-Trøndelag Health Study (The HUNT Study) is one of the largest population health studies ever performed. It is a unique database of questionnaire data, clinical measurements and samples from a

county's inhabitants, collected in four periods of time: HUNT1 (1984-86), HUNT 2 (1995-1997), HUNT3 (2006-2008) and HUNT4 (2017-2019).

Methods: The study is approved by the local ethics committee and comply with local GDPR-guidelines. 750 patients with G12-code in the ICD-10 or similar codes in the previous ICD-9 have been in the hospital administrative systems, and we expect between 500-600 real cases when duplicates and errors are removed. All journals will be read and diagnosis verified. An eCRF has been developed for the purpose of registering variables on disease progression, phenotype and care provided.

We expect a total number of 157 patients identified in the patient administrative system to have participated in the HUNT study. Variables concerning cardiovascular risk factors, environmental exposures and (in a smaller cohort of 80 genetics) will be compared to the non-ALS-population in the HUNT studies.

Results: Results will be presented at the meeting.

Discussion and conclusions: Will be presented at the meeting.

WP-05 Assessing structural- and copy number- variation in MND

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Keywords: bioinformatics, SALS, copy number variation

Background: Gene mutations are the only proven cause of MND. Yet, 40% of familial MND still carry unknown gene mutations. Most genetic risk factors that underlie sporadic MND also remain to be identified. Structural changes in DNA are known to cause other neurological diseases but these changes are yet to be widely studied in MND.

Objectives: The objectives of this project are to identify and catalogue structural- and copy number- variation (SV/CNV) that contribute to the genetic aetiology of MND. A comprehensive catalogue of structural variation is being generated by bioinformatic analysis of available whole genome sequencing (WGS) data from MND patients. The SV/CNV catalogue will be interrogated using both a candidate gene approach and a genome-wide unbiased screen to identify disease-associated SV/CNVs in MND.

Methods: We have previously generated WGS data from 628 SALS cases, nine individuals from four monozygotic twin sets (one triplet set) discordant for MND and nine individuals from three MND families with unknown gene mutations. Two bioinformatics tools, CNVnator and Lumpy are being used to identify SV/CNVs in the MND and control datasets, both of which have been found to out-perform other available tools. As both tools produce differing SV/CNV calls, a third program, MetaSV is utilised to reduce false-positives and produce a list of high-quality, high-confidence SV/CNV calls. The SV/CNV catalogue will be interrogated for variation that may be associated with sporadic MND when compared to controls. In this case, the frequency of all SV/CNVs present in cases and controls will be compared to identify association. Control cohorts include in-house filtering through the Project MinE and

Australian MGRB datasets, and interrogation through the DGV database of 60,000 CNVs from healthy controls. All candidate SV/CNVs identified will be manually validated in the laboratory.

Discussion and conclusions: This comprehensive analysis of SV/CNVs in Australian MND seeks to identify additional mutations that cause, increase risk, or affect phenotypic traits of MND and provide greater understanding of the complex genetic aetiology of MND. The identification of disease-associated SV/CNVs will also have significant clinical outcomes. The identification of MND-causative SV/CNVs in families will enable development of additional genetic testing including pre-implantation embryonic screening (PGD). In the future, SV/CNVs that are found to confer risk to developing or are protective against MND have potential to inform clinicians in predicting disease progression. In addition, these variants may inform patient and clinical stratification for better informed clinical decision making and enhanced strategies for testing potential therapies.

Acknowledgements: MNDRIA Peter Stearne familial MND Research grant, NHMRC grant 1083187

WP-06 Long-read sequencing approaches to investigate the contribution of human-specific variable number tandem repeats to ALS susceptibility

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Keywords: genetic modifiers, WGS (whole genome sequencing),

Background: The hexanucleotide repeat in C9orf72 is one of over 30 tandem repeats

that when expanded can lead to neurodegenerative disease. However, this number is a small fraction of the more than 70,000 tandem repeats that are present in the human genome. Many of these repeats have been understudied, in part, because they are technically hard to amplify, especially ones with a large internal repeat unit. These repeats are also not covered effectively by whole genome sequencing techniques thereby necessitating targeted and/or long-read sequencing. The genetic composition of ALS is far from complete and large repeat expansions may explain some of this missing genetic heritability in a manner analogous to C9orf72 repeat expansions.

Objectives: We sought to ascertain the distribution of tandem repeats with a focus on human-specific repeats present in exons or introns of known genes. We hypothesize that genetic variation in these regions can contribute to ALS susceptibility.

Methods: Our selection criteria included tandem repeats with a high degree of variability in humans in a region that is fixed in length or absent in non-human primates. We prioritized repeats in brain-expressed genes and in regions that could influence alternative splicing. Whole genome sequence data was obtained from the Answer ALS consortium. We estimated repeat length by calculating read depth across repeats compared to adjacent genomic segments. We then employed the same procedure for >2500 samples from the 1000 Genome Project samples to identify repeats that had increased length in ALS samples. Candidate repeats were confirmed by multiplexed PacBio single-molecule real-time sequencing in patient samples with ALS and control individuals, obtained from the Coriell Institute.

Results: We identified a set of 25 candidate repeats that demonstrated a striking variability in repeat length distribution across patients with ALS and control individuals. Of these, we selected three repeats for follow-up using PacBio long-

read sequencing. Our targeted sequence depth of coverage allows us to ascertain the exact repeat length and internal nucleotide composition, features which may be critical to influencing disease susceptibility.

Discussion and conclusions: We are establishing a pipeline for a genome-wide approach to identify novel potential contributions of repeat expansions to the development of ALS. As technologies for long-read sequencing mature, we are obtaining a clearer picture of regions of the human genome that were previously difficult to sequence and warrant investigation in the context of ALS.

WP-07 Novel patient-derived 3D *in vitro* models of microglia to study neuroinflammation in ALS

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Keywords: microglia, disease modeling, 3D culture

Background: Despite intense research efforts on understanding ALS mechanisms to identify potential pharmacological targets, no effective disease-modifying therapies have yet successfully translated to the clinic. This, in part, stems from the incomplete characterisation of the role of neuroinflammatory responses in inducing or protecting motor neurons from progressive degeneration. Microglia, the brain-resident immune cells, are crucial mediators of neuroinflammation in ALS and other brain diseases. However, current microglia models using animal and *in vitro* systems do

not accurately recapitulate the features of human adult microglia in a disease- and patient-specific manner. As a result, such models are not able to predict clinical success.

Objectives: To overcome the limitations of current animal and cell-based systems in modelling microglia-mediated responses and drug action in ALS, we aim to develop a more clinically-relevant human *in vitro* model of ALS by generating novel patient-derived 3D cell culture platforms.

Methods: Human microglia-like cells were generated by cytokine (IL-34 and GM-CSF)-mediated differentiation of peripheral blood-derived monocytes¹ from ALS patients and age-matched healthy controls. Hydrogel-based 3D cultures of microglia-like cells were obtained by embedding monocytes in Matrigel for 40 days. Neurons and astrocytes derived from spontaneously differentiated ReNcells (human immortalised neural progenitors) were co-cultured with microglia-like cells in Matrigel-based 3D cultures.

Results: Our preliminary data showed that monocyte-derived microglia-like cells have ramified morphologies resembling brain-resident microglia and significantly ($P < 0.05$, $n = 5$) express higher levels of microglia-specific markers compared to monocyte-derived macrophages. Upon growth in Matrigel-based 3D cultures, monocyte-derived microglia-like cells survived longer ($P < 0.0001$, $n = 7$) compared to 2D cultures. Overall, the morphology of microglia-like cells from ALS patients and age-matched healthy controls grown in 3D was significantly more complex, with higher branched patterns and more cell processes than 2D cultures. Interestingly, we observed morphological differences between microglia-like cells grown in 3D from ALS patients with either a rapidly or a slowly progressing form of the disease, that were not recapitulated in 2D. To better represent the neuro-glial microenvironmental cues where microglia grow in the brain, we cultured ALS and age-matched healthy

control microglia-like cells in the presence of ReNcells in 3D co-cultures. Experiments are underway to further characterise ALS-associated microglial phenotypes in 3D co-cultures with ReNcells.

Discussion and conclusions: Clear morphological differences between monocyte-derived microglia-like cells grown in 2D and 3D cultures were observed regardless of the disease state, being microglia cultured in 3D more complex. This suggests that providing 3D growth conditions can improve current cell models of human microglia. Also, co-culture with other brain cells in 3D might favour a more accurate representation of microglia-associated responses in ALS brains.

Acknowledgements: We thank volunteers for taking part in the study. Funding was provided by MNDRIA from Col Bambrick MND Research Grant and the University of Queensland.

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WP-08 NF-kB activation in astroglia in mouse models of ALS

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Keywords: astrocyte, microglia, NF-kappaB

Background: Despite intensive research efforts the disease pathomechanisms of ALS remain poorly understood. Mutations identified in familial forms of ALS are used in murine models and mimic key aspects of ALS. In recent years, the contribution of

non-neuronal cells in the disease progression has been recognized. Our group identified that early activation of NF-kB signaling in astrocytes delays the onset of symptomatic ALS, while late activation accelerates the disease progression in the SOD1G93A model of ALS. Early expansion of microglia coincides with the activation of NF-kB signaling in astrocytes and we identified WNT signaling as a possible mediator microglia expansion.

Objectives: We aim to further elucidate the function of NF-kB signaling in the pathogenesis of ALS. We expand our model of astrocytic NF-kB activation in ALS models with genetic ablation of WNTs and pharmacological depletion of microglia. First, we want to identify early microglia expansion as a beneficial event in ALS pathogenesis and investigate astrocytic WNT signaling as a mediator of microglia expansion. Second, we want to verify the profound impact of NF-kB activation on disease progression in a TDP-43 model of ALS.

Methods: First, the established SOD1G93A ALS model will be combined with astrocytic Doxycycline-inducible activation of NF-kB signaling and microglia will be pharmacologically depleted by PLX3397 treatment. Second, we will examine the impact of astrocytic WNT on microglia expansion by combining the astrocytic NF-kB activation with astrocytic genetic deletion of WNTs. Third, we will assess the impact of astrocytic NF-kB activation in a TDP-43-dependent model of ALS. These murine models will be thoroughly studied by behavior and motor testing as well as histological and biochemical analyses of brain and spinal cord tissue.

Results: In the past we could show that astrocytic NF-kB activation attenuates disease progression of the SOD1-G93A model and identified astrocytic WNT signaling as mediator of microglia expansion. Continued NF-kB activation delayed disease onset but accelerated disease progression after onset (1).

Interestingly, NF- κ B activation during the presymptomatic phase improved survival and delayed onset as well (1). We are currently expanding our understanding of the role NF- κ B in ALS as outlined above.

Discussion and conclusions: Our studies provide first evidence that bolstering of the presymptomatic immune response is a viable treatment option for ALS patients.

Acknowledgements: We thank B. Knöll, F. Roselli and A. Ludolph for their continued support.

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WP-09 Good riddance to bad rubbish: Waste disposal in human ALS post mortem pericytes

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Keywords: autophagy, TARDPB/TDP-43, Ubiquitin proteasome system

Background: TDP-43 aggregates are found in motor neurons of post mortem ALS tissue in 97% of cases (1)(2). Genetic mutations in protein degradation pathways eg VCP in autophagy and SQSTM1 in the ubiquitin proteasome system cause ALS (3), and are likely responsible for the accumulation and aggregation of TDP-43. The field is divided regarding which degradation system is impaired in ALS (4). Additionally, 50% of pericytes, cell components of the blood brain barrier are lost in post mortem ALS patients (5). Whether the loss of pericytes, like the loss

of motor neurons, involves impairment of protein degradation is currently unknown.

Objective: To determine if pericytes from human post mortem ALS patients show impairment in the degradation of TDP-43, and whether that impairment relates to autophagy or the UPS. Evidence of impairment in either degradation system in pericytes would identify pericytes as a target cell type for therapeutics that augment protein degradation in ALS. In addition, pericytes could then be used as a screening model for such therapeutics.

Methods:

1. Degradation of TDP-43: TDP-43 is fused to a tandem fluorescent timer consisting of two fluorophores that mature at different rates. The ratio of the slowly maturing mCherry to the fast maturing sfGFP indicates the ratio of older to younger TDP-43; a ratio we predict will be higher in cells with protein degradation impairment. Human ALS and control pericytes are transduced with the TDP-43 tandem fluorescent timer and the intensity of each fluorophore is measured over time in single cells.
2. Autophagy: Measuring the ratio of LC3-II, a substrate and component of the autophagy system, to its precursor LC3-I, and the abundance of the autophagy substrate p62, by western blot indicates if there is an impairment in autophagy in ALS versus control human pericytes.
3. Ubiquitin proteasome system (UPS): The activities of the 3 caspase sites of the proteasome: trypsin-like, caspase-like and chymotrypsin-like are measured by adding luminogenic substrates for each individual site and measuring the resulting luminescence.

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WP-10 Investigating TDP-43 mislocalisation using novel human induced pluripotent stem cell models

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Keywords: TARDBP/TDP-43, human iPSC

Background: TDP-43 cytoplasmic mislocalisation is a common and unifying histological feature of ALS pathology. TDP-43 positive inclusions appear in a majority (>95%) of amyotrophic lateral sclerosis (ALS) cases, despite TDP-43 gene mutations occurring in relatively few familial or sporadic cases. This suggests that TDP-43 mislocalisation is central to the mechanism of neurodegeneration in all forms of ALS. Our goal is to create a new model of ALS, by using human induced pluripotent stem (iPS) cells and

CRISPR/Cas gene editing techniques to disrupt the function of the TDP-43 gene. We are testing complimentary approaches to this, and are pursuing i) a 'knock-in' approach in which the TDP-43 open reading frame, either normal or with a mutated nuclear localisation sequence, is engineered into the human AAVS1 locus, and ii) an approach in which the autoregulatory domain within the 3'-UTR of the endogenous TDP-43 gene is disrupted. Concomitant with this work, we have been pursuing strategies to study exosome release and transmission using compartmentalised microfluidic cultures, and 3-dimensional (3D) cerebral organoid cultures. For the latter, we have used 3D printing to make bespoke mini-bioreactors for cerebral organoid culture, which significantly reduce the amount of medium required per organoid, allowing us to undertake a more comprehensive analysis of the effects of TDP-43 mislocalisation. Progress on the development and characterisation of these novel human iPS cell-based models of TDP-43 mislocalisation will be presented; such a model may have particular relevance for modelling sporadic forms of ALS.

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WP-11 Characterising CYTSB as a potential therapeutic target for organ pathology in Spinal Muscular Atrophy

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Keywords: SMA, therapeutic strategies, organ pathology

Background: Spinal Muscular Atrophy (SMA) is a devastating autosomal recessive disease characterised by progressive muscle weakness and paralysis. Children with the most severe form of SMA never sit unassisted and often face high rates of early mortality. There is currently no cure for SMA, however recently a therapy has been approved which, like many therapies currently under development, targets the major neuromuscular symptoms of the disorder. Increasing evidence suggests SMA is a multi-organ disease. More comprehensive therapies are therefore required, targeting organ pathologies alongside the neuromuscular symptoms. Genes under epigenetic control have not yet been explored in SMA research. Epigenetic modifications such as methylation are known to regulate processes such as tissue-specific expression and differential splicing, both known to be important in SMA pathogenesis. CYTSB is a gene demonstrated to have significantly altered methylation in SMA patients. Correspondingly, CYTSB expression is increased in SMA mouse livers at pre-symptomatic postnatal day 0. We characterise the expression of the CYTSB gene and protein across several healthy and SMA tissues, to establish its suitability as a potential therapeutic target.

Acknowledgements: We would like to thank Tenovus and the Carnegie Trust for funding this project, as well as our collaborators at the University of Edinburgh and the University of Strathclyde.

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WP-12 A combined structural, functional and neurochemical MRI signature of motor system excitability in ALS

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Keywords: MRI/MRSI, biomarker, C9orf72

Background: Biomarkers of disease activity remain a key unmet need in ALS to establish therapeutic efficacy in clinical trials. A multimodal approach is necessary in an expanding clinical and molecular syndrome to allow for precision medicine. Using paired-pulse transcranial magnetic stimulation (TMS), reduced physiological short-interval cortical inhibition is consistently demonstrable in ALS. MRI is another non-invasive approach that can be applied to evaluate cortical excitability, yielding quantifiable structural and functional motor system biomarkers. Novel MR spectroscopy (MRS) approaches have been developed to allow integration of motor cortex neurochemistry (including GABA and glutamate).

Methods: Individuals with ALS (sporadic and familial) are recruited to a biomarker cohort study based in a large tertiary ALS clinic. Asymptomatic first-degree relatives of familial ALS patients are also offered participation (remaining blind to their genetic status). Additional healthy controls are recruited from patient spouses and unrelated volunteers. A multimodal MRI protocol is conducted on a Siemens 3T scanner, including T1, DTI, FMRI, and MRS using a region-of-interest spanning both motor cortices. TMS and

magnetoencephalographic data are also acquired.

Results: Comparison of MRI data from the first 5 affected ALS (4 sporadic, 1 *C9orf72*) versus control participants revealed characteristic reduced fractional anisotropy (FA) in the body of the corpus callosum and left corticospinal tracts of patients; plus increased ipsilateral motor cortex and bilateral temporoparietal fMRI activation in relation to a unilateral motor task, performed with both hands in turn. In first-degree relatives (n=5) of individuals with ALS caused by *C9orf72*, there was a trend towards an excitatory neurochemical profile, with increased glutamate and reduced GABA.

Discussion and conclusions: This successful application of sequences ultimately applicable to the clinical environment strengthens the potential of MRI as source of sensitive and specific biomarkers in ALS. A multi-parametric neuroimaging and neurophysiological approach to motor system activity in symptomatic and, in due course, pre-symptomatic gene carriers will allow key pathogenic pathways to be characterised. It will also address the aim of quantifiable biomarkers for the assessment of emerging therapeutics such as oligonucleotides, including aspirations for their eventual preventative application.

WP-13 Diagnostic utility of the split-hand index in ALS phenotypes

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Keywords: disease subtypes, neurophysiology, split-hand index

Background: Preferential wasting of the thenar group of muscles, the split hand sign, has been long described as pathognomonic of amyotrophic lateral sclerosis (1) (ALS). The split-hand index (SI) (2) based on this clinical phenomenon was seen to be a robust, widely available, diagnostic tool which differentiated ALS from mimic disorders.

Objectives: To confirm the diagnostic utility of the SI in a large group of ALS phenotypes. Assess, differences in SI between the onset and the contralateral side hand in lateralized ALS and between the dominant and non-dominant hand in non-lateralized disease onset. Assess the utility of SI in PLS and pyramidal ALS.

Methods: Four hundred patients with varying ALS phenotypes diagnosed by the Awaji criteria (3) underwent measurement of the SI from both hands. Calculation of the SI was performed as previously described (2). Clinical and functional assessments were undertaken in all patients with a subset of patient undergoing progress SI measurements. Results for the SI were compared with 126 neuromuscular controls (2). Means of SI between groups was performed using student T test while correlation of SI with clinical measures was performed using the Spearman's correlation.

Results: Previous studies in 44 ALS patients established the significant reduction of the SI in all ALS patients with robust diagnostic utility of a diagnostic cut-off value of 5.2 in limb onset ALS. SI from both sides and clinical data for four hundred ALS patients in the current study is being analysed in the subgroups of bulbar, upper limb and lower limb onset ALS, along with pyramidal ALS and PLS patients. This is to

determine the correlation of a diagnostic value of SI with the sign of symptom onset in lateralized disease, or the dominant side in non-lateralised disease, along with the diagnostic utility of SI in PLS and pyramidal ALS phenotypes.

Discussion and conclusions: The split-hand index is a widely available and simple diagnostic tool that can aid the clinical diagnosis of ALS. Assessment of the diagnostic utility and limitations of the SI in a large cross section of ALS patient phenotypes and in a subset of patients with prospective serial studies would help clarify the diagnostic and prognostic utility of the SI in ALS phenotypes.

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WP-14 People living with ALS and their caregivers' input into drug development in Europe

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Keywords: drug development, disease burden, patient-focused

Background: There is a need for rigorous patient input into key areas of drug development, regulatory consideration and definition of clinically meaningful outcomes. There is also an emerging focus on patient engagement in determinations of value for health system utilization and payment.

There is a critical opportunity to use established methods to ensure that patient input is appropriately integrated into drug development. A European survey of people with ALS and caregivers will collect data on the burden of disease with emphasis on the loss of function over the course of the disease. The European Medicines Agency (EMA) is considering methods to better incorporate patient and caregiver input into regulatory review processes. Given the potential for EMA review of several new ALS therapies over the coming years, it is important for the community to develop this type of information.

Objectives: To survey European ALS patients and in-home caregivers to capture the burden of that condition, across approximately 10 countries. Patients and their primary caregivers may have different perceptions and concerns regarding the burden of disease. The survey will allow for comparisons of perspectives, and capture how these perspectives change during ALS progression for patient subgroups. In addition results of this survey will allow comparison with results from a 2017 US survey.

Methods: A steering committee was established, consisting of industry partners, clinical and methodological experts, with input from patients and caregivers. The survey materials used in the US were adapted for use in Europe and most questions are directly comparable. Recruitment of patients and caregivers will be carried out with the partnership of European Network for the Cure of ALS (ENCALS) and advocacy groups in each

country. A representative sample of patients and caregivers across disease severity, demographics and regional areas will be targeted.

Results: Descriptive statistical analysis of European patient and caregiver data, and free text analysis of open ended responses. The survey results will also be analyzed in conjunction with the results of a similar survey carried out in the United States.

Discussion and conclusions: The ALS patient and caregiver surveys in Europe will provide information on the disease burden from both perspectives and provide guidance into drug development processes.

Acknowledgements: The IMPACT European Survey Advisory Group: Christopher McDermott, Steve Bell, Judith Newton, Leonard van den Berg, Garrit-Jan Blonk, Jesus Mora Pardina, Phillip Van Damme, Evy Reviere, Danny Reviere (patient), Mia Mahy (caregiver), Dorothee Lule, Francois Salachas, Caroline Ingre, Lucie Bruijn.

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WP-15 Lived experience of patients with amyotrophic lateral sclerosis who participated in a clinical trial

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Keywords: clinical trial, qualitative study, support

Background: Currently only riluzole and edaravone are approved for the treatment of ALS (1). With only two therapies approved

for a devastating disease, clinical trials are crucial for the development of new drugs. Patient participation in clinical trials is vital to progress the development of potential therapies. Studies have looked at the barriers and facilitators to recruitment, both from the patient and physician perspective (2, 3); however there remains a lack of knowledge on a patient with ALS' lived experience during their participation in a clinical trial. As the physical effects of ALS can already take a grand toll on a patient's well being, it is essential to understand what factors contribute to patients completing a clinical trial to its entirety.

Objectives: To study a patient with ALS' motivation during their participation in a clinical trial and the factors that contribute to their participation.

Methods: This will be an observational longitudinal study. Approximately 15-20 patients will be recruited. Only those who have completed a clinical trial to its entirety will be eligible to participate. A semi-structured interview will be conducted with each patient.

Discussion and conclusions: Themes extracted from the data analysis will provide greater insight into a patient's lived experience during a clinical trial, and in particular, what keeps them motivated. With this information, the clinical team can better prepare patients entering a trial, as well as potentially better address patients' concerns about participation in clinical trials.

Acknowledgements: ALS Multidisciplinary clinic - Montreal Neurological Institute and Hospital.

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WP-16 Phase 1/2a, Double-blind, Placebo-controlled Study with an Open-label Extension of Ropinirole Hydrochloride Extended-Release Tablets (ROPALS trial based on the iPSC drug repositioning)

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Keywords: iPSC, drug target, drug repositioning

Background: Our laboratory previously established spinal motor neurons (MN) from induced-pluripotent stem cells (iPSCs) prepared from both sporadic and familial ALS patients and successfully recapitulated disease-specific pathophysiological processes. We next searched for effective drugs capable of slowing the disease progression of ALS using a drug library of 1232 existing compounds and discovered that ropinirole hydrochloride prevented MN death. In December 2018, we started an investigator-initiated clinical trial testing ropinirole hydrochloride extended-release tablets in ALS patients.

Objectives: This is an on-going phase I/IIa randomized, double-blind, placebo-controlled, single-center, open-label continuation clinical trial (UMIN000034954). The primary aim is to assess the safety and tolerability of ropinirole hydrochloride in patients with ALS. Secondary aims include several evaluations of effectiveness: ALS functional rating scale-revised (ALSFRS-R), quantitative muscle strength, muscle volume, survival, and ALSAQ40 scale. We will also perform an efficacy evaluation using subjects-derived iPSCs/MN.

Methods: The major inclusion criteria were as follows: 1) “clinically possible and laboratory-supported ALS”, “clinically probable ALS” or “clinically definite ALS” according to the criteria for the diagnosis of ALS (El Escorial revised) and within 60 months after disease onset; 2) Grade 1 or 2 according to the ALS Severity Classification; 3) Japanese patients between 20 and 80 years of age; 4) ALSFRS-R score ≥ 2 points for all items; 5) %FVC $\geq 70\%$; 6) written informed consent for participation in the study; 7) able to be treated in an outpatient setting; and 8) change in ALSFRS-R score of -2 to -5 points during the 12-week run-in period.

Results: At present, a total of 23 patients have been successfully recruited; 12 of these patients (8 men) are enrolled in the 24-week double-blind phase. At enrollment, the mean \pm SD disease duration of the 12 patients was 19 \pm 11 months. The mean \pm SD ALSFRS-R score was 44 \pm 2, with a mean reduction of -3 points. The remaining 11 patients are presently in the 12-week run-in period. Finally, 15 patients will be assigned to the active drug and 5 patients to the placebo. The results will be known in March 2021.

Discussion and conclusions: Our trial will be a touchstone trial for iPSC-based drug development strategies and will provide reliable and important data.

Acknowledgements: This study was supported by Japan Agency for Medical Research and Development (AMED), K Pharma, Inc and GlaxoSmithKline plc. Dr. Okano has received personal compensation for consulting, serving on a scientific advisory board, speaking, or other activities with K Pharma Inc., and SanBio Co. Ltd. Dr. Okano has received compensation for serving on the Board of Directors of SanBio Co.Ltd. Dr. Nakahara has received honoraria from Biogen, Mitsubishi-Tanabe, Novartis, and Takeda; and served as a paid scientific advisor to Biogen, Novartis and Takeda.

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WP-17 The Japanese Early-Stage Trial of High Dose Methylcobalamin for Amyotrophic Lateral Sclerosis (JETALS): Protocol of the phase III trial and validation of the updated Awaji criteria for the diagnosis of early stage ALS

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Keywords: clinical trial, trial design, methylcobalamin

Background: In our previous study (E0302-J081-761) conducted to verify efficacy and safety of high dose methylcobalamin against patients diagnosed by the revised El Escorial criteria (rEEC) within 36 months from onset, no significant differences were detected in the time interval to survival events and changes in the Revised ALS Functional Rating Scale (ALSFERS-R) score from baseline to week 182 (minimal p value = 0.087). However, post-hoc analyses suggested that methylcobalamin may prolong survival and retard symptomatic

progression without major side effects if started early (≤ 12 months' duration) (1).

Objectives: We planned to conduct the Japanese Early-stage Trial of high dose methylcobalamin for Amyotrophic Lateral Sclerosis (JETALS) as an investigator-initiated trial to confirm the efficacy and safety of methylcobalamin 50mg for ALS patients within 12 months after the onset (E0302-J081-763) (2)

Methods: JETALS is a prospective, multicenter, placebo-controlled, double-blind, randomized phase III study conducted at 25 tertiary neurology centers. Patients diagnosed with ALS corresponding to the categories of definite, probable, or probable-laboratory supported in the updated Awaji criteria (UAC) within 12 months from onset were registered at observation period, then patients whose ALSFRS-R total score has decreased by 1–2 points during 12 weeks proceeded to the treatment period and were randomized at a 1:1 ratio to receive intramuscular injection with methylcobalamin 50mg or placebo twice a week for 16 weeks. We adopted UAC for the first time in the world to our knowledge, which revealed a higher sensitivity compared to rEEC (3). The target number of subjects is 128. The primary endpoint is changes in the ALSFRS-R total score at 16 weeks.

Results: This study was started in October 2017 and is currently in progress. By the end of May 2019, 178 and 100 patients have been enrolled at observation period and treatment period, respectively. The transfer rate from observation to treatment period has been 67%. Of 18 patients entered at observation period in Tokushima University Hospital, which is a supervision institute of this trial, only 9 patients corresponded to the categories of definite, probable, or probable-laboratory supported in the rEEC.

Discussion and conclusions: Registration (in progress) is on schedule. UAC may

contribute registration for early stage ALS patients.

Acknowledgements: This work is funded and supported by the Japan Agency for Medical Research and Development under the agency's Practical Research Project for Rare Intractable Diseases (project number: 19ek0109252h0001). The investigational product is provided by Eisai Co., Ltd.

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WP-18 Clinical characteristics of young-onset amyotrophic lateral sclerosis in Korean cohort

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Keywords: disease onset

Background: Amyotrophic lateral sclerosis (ALS) is the neurodegenerative disease characterized by the progressive degeneration of motor neurons. ALS is most frequent (approximately over 50%) motor neuron disease and has nearly 3 years of mean survival time in Korean nationwide epidemiologic study of ALS (Jun et al., JNNP, 2018). Comparing the survival time to the age at onset in the study, the survival time in the young-onset group (<40 years) was much longer (57.7 months) than the survival time in the older group (≥ 60 years, 31.4 months). Following the result, young-

onset ALS is suggested to have different features rather than the older age group. However, young-onset ALS has an arbitrary cut-off age of 40 or 45 years, varying to the studies (Sabatelli et al., 2008; Turner et al., 2012).

Objectives: The aim of this study was to identify the characteristics and prognosis of young-onset ALS from one of the largest ALS/MND cohorts in Korea.

Methods: To determine the cut-off age of young-onset ALS, this study expected age of onset from the Korean epidemiologic study. In this study, young-onset ALS was defined as ALS that occurs before the age of 35.6 years.

158 patients with age at onset below 35.6 years were registered Hanyang MND cohort from January 2002 to November 2018. Among them, the remaining 55 Korean young-onset ALS patients who meet revised El Escorial criteria with sufficient information were finally recruited in this study.

For the comparison of characteristics and prognosis of young-onset ALS, study population during 1 year (2011.03.01-2012.02.28) was selected. Among them, 142 patients who met revised El Escorial criteria with sufficient information and started the first symptom after 35.6 years were recruited in this study as a control group, Adult-onset ALS.

Results: With identifying family history and genetic testing of young-onset ALS, three patients with family histories (5.5%, 3 of 55) were classified familial ALS and four patients (7.3%, 4 of 55) with pathogenic or likely pathogenic variants, of ALS causative or susceptibility genes, were identified. In adult-onset ALS, there is no familial ALS but eleven patients with the genetic variants (7.7%, 11 of 142). Comparing the characteristics, disease duration before diagnosis was longer in the young-onset ALS rather than adult-onset ALS (20.6±16.3 months, vs 11.8±14.2 months [mean±SD], p<0.01). Bulbar-onset ALS was uncommon

in young-onset ALS than adult-onset ALS (14.5% vs 34.5%, $p = 0.02$) and cognitive impairment was less in young-onset ALS than adult-onset ALS (21.1%, 8 of 38 vs 46.5%, 40 of 86, $p = 0.02$). Progression from diagnosis to latest follow-up was slower in young-onset ALS than adult-onset ALS (0.75 ± 0.81 , 0.00-4.13 vs 1.14 ± 1.13 , -1.50-6.00 [mean \pm SD, range], $p = 0.02$). Comparing survival time, young-onset ALS survival is much longer than adult-onset ALS (9.4 years vs 4.8 years [median], $p < 0.01$).

WP-19 Machine learning for novel prognosis prediction and ALS patient stratification

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Keywords: machine learning, prognosis model

Background: Heterogeneity in ALS patient population is a significant burden for proper clinical trial design and adequate patient care. These two issues have undergone extensive research in recent years due to the increasing availability of large patient databases. Machine learning methods have emerged as key with regards to understanding the underlying patterns in data. Previous research has focused on predicting survival rate and functional loss. Past stratification schemes were confined to

a narrow experimental setup and were strongly restricted by the investigation scope.

Objectives: Our work proposes an alternative approach to prognosis modeling and patient stratification. Efficient data pre-processing is carried out to deal with dimensionality, missing data and censoring. Prognosis is evaluated using a novel prediction metric and unsupervised machine learning methods are carried out on the patient population.

Methods: Clinical trial and real life patient datasets were used so as to compare model performance on both populations. Clinical trial patients came from PRO-ACT, a publicly available database which aggregates more than 23 clinical trials, Trophos and Exonhit. Real life patients originate from Paris' Pitié Salpêtrière ALS center (APHP) and regional Tours and Limoges ALS centers in France.

Results: PRO-ACT, Trophos and Exonhit databases include 10 700, 500 and 400 patients respectively. Patient monitoring ranges between 12 to 18 months. Vital signs, ALSFRS scores, riluzole intake, labs results, muscular testing are available in varying manners for each patient. The real life patient database from the Pitié Salpêtrière aggregate more than 5 700 patients monitored between 1989 and 2008. Regional ALS center (Tours, Limoges) respectively include 500 and 700 patients. Vital signs, riluzole intake, ALSFRS, muscular testing, detailed clinical onset description and labs results are available for a major part of the population. Prognosis prediction and patient stratification results will be presented during the Symposium.

WP-20 Intranasal oxytocin for terminal ALS with social interaction deficits

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Keywords: communication, ALS-FTD, oxytocin

Background: Patients with terminal ALS sometimes demonstrate abnormalities in behaviour and social cognition. This is a serious problem for both patients and caregivers, and there are currently no established treatments for empathy deficits. Evidence on the efficacy of psychological treatment of terminal ALS is strongly needed. The synthetic hormone oxytocin is a potential treatment option to improve the core social and behavioural difficulties in these patients, but its efficacy has yet to be evaluated in young children who may benefit to a greater extent. Previous research showed that oxytocin improved the core social and behavioural difficulties of patients with behavioural variant frontotemporal dementia, which has a common transactivating response region DNA binding protein-43 with terminal ALS with behavioural variant frontotemporal dementia. Therefore, we hypothesized that oxytocin could be effective for the management of the social behaviour and social cognition abnormalities in terminal ALS patients.

Objectives: The aim of this small clinical trial was to determine the safety and tolerability of intranasal oxytocin and to identify the use of oxytocin for individuals with terminal ALS.

Methods: Three patients with terminal ALS and who had problems in behavioural and social cognition participated in this trial. We administered intranasal oxytocin (24 IU/mL) once daily for 1 week, followed by a washout period of 1 week, before repeating two cycles. Using an intervention controlled before-after study, we investigated the efficacy, tolerability, and safety of oxytocin treatment in patients with terminal ALS.

Results: Intranasal oxytocin was not significantly associated with adverse events. In all patients with terminal ALS, oxytocin was well-tolerated, improved the short quality of life scores; and had short-term benefits on behavioural symptoms.

Discussion and conclusions: Intranasal oxytocin appeared to improve the social aspects of cognition and behavioural symptoms in individuals with terminal ALS. This small clinical trial was the first case pilot study to support the potential of oxytocin in improving the social interaction deficits of patients with ALS. Further clinical trials are warranted to determine the therapeutic efficacy of long-term intranasal oxytocin for the behavioural symptoms of terminal ALS.

Acknowledgements: We would like to thank the patients for taking part in this study. Our research was approved by the ethics committee of the institution.

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WP-21 Assessing assistive technology use and needs by individuals with ALS/MND

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Keywords: assistive technology, clinical care

Background: Individuals with ALS/MND often require assistive technology for mobility, to communicate, or to access their computer or environment. The assistive technology available is ever evolving. We have resources to provide hands-on trial and loan of equipment within the framework of routine medical care at the multidisciplinary team clinic visit. While implementing this, we found differences in peoples' understanding of what assistive technology is available and what that assistive technology is capable of. We were first interested in collecting data on what people are currently using, but found we also wanted to collect expectations and ideas.

Objectives: The goal of this study is to gauge the current assistive technology use and needs of people living with ALS/MND. This data will determine the level of familiarity and effectiveness of this technology as well as provide direction for the development of new technologies to assist people with disabilities.

Methods: This study involves a questionnaire answered by people with ALS/MND and includes multiple sections with questions regarding devices for communication, computer access, and mobility, plus additional assistive technology queries. The responses collect data on use and knowledge of assistive devices. Age, gender, and diagnosis are also collected.

Results: To date, we have had 46 people complete the survey: 30 Male/16 Female; Age 35-84 (Med 61). We continue to collect data, but here is a sample of the use responses so far: 1) 8/46 (17%) use a communication device, 2) 33/46 (72%) use a computer. 5/33 (15%) use alternative access to use their computer, 3) 32/46 (70%) use a mobility device.

Here is a sample of the needs question: Is there anything that your current devices are not capturing in terms of function that you wish they could?

Answers: Independently lift a person up off the ground if they fell; Easier to use bathroom; Speaking on phone; Exoskeleton for walking; Putting on make-up; Arm raisers for chairs that can be attached; Upright power wheelchair; TV remotes accessed by voice; Become one with the machine, just like a motorcycle; Arm cushion; A device that's good for both inside and out; Being able to carry things; Transportation; Climb stairs; Tilt forward.

Discussion and conclusions: The data collected to date is both interesting and informative. With the addition of more responses, we will be able to ascertain a full catalogue of what assistive technology is currently being used by our population as well as find those needs that remain unmet by technology. We will present on our full data set.

WP-22 The addition of rotational and adjustable flexion components to cervical support

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Keywords: clinical care, symptom management, cervical support

Background: Individuals with amyotrophic lateral sclerosis/motor neuron disease (ALS/MND) often present with cervical weakness resulting in the inability to hold their head upright. The standard of care is to recommend a cervical support, often a rigid collar, to compensate for this weakness. Current cervical orthotics are designed to provide stabilization and to restrict movement within the collar. Not all individuals with neck weakness need this

level of confinement or tolerate the strict positioning. The addition of a rotational piece would allow for freedom of movement of axial rotation; the addition of an adjustable angle chin piece would allow for customized flexion/extension settings.

Objectives: The goal of our project was to adapt an already available neck brace/collar, capable of establishing neutral head position, to 1) allow for rotational movement with minimal effort, and 2) to provide a customizable option to optimally position in flexion/extension. This custom design must be not only functional, but also comfortable. It must also include an efficient use of time, materials and money.

Methods: The team consisted of people living with ALS (PALS), healthcare professionals (OT, PT, SLP) and designers (Biomedical Engineering students, 3D printer coordinator). Commercially available products as well as previous prototypes were reviewed by the team and a novel design concept was developed.

The initial model was fabricated using thermoplastic splinting material and a commercially available rigid collar. The thermoplastic material was used to cover the collar and provide a base for the chin piece. The chin piece was a shorter piece of the same material and encircled the base. It is able to easily slide over the base piece allowing for rotation.

The adjustable piece was designed with a gear-like axis to allow flexion and extension for both comfort and ideal positioning.

Results: The review of the prototype design of the rotational piece was very positive. The ability for smooth rotation due to the decreased friction between the materials was a key feature. It was during the preview of this prototype that the request for the adjustable angle was made. We are currently in the design phase of adding on this feature. The use of the thermoplastic material in the prototype will also be

upgraded to a 3D printed version for cosmetic reasons.

Discussion and conclusions: The design intent of this project is to improve upon the current neck support systems by providing more dynamic maneuverability and customization while continuing to provide the support needed. The current prototype that allows for rotation fulfills the first objective, and we are working on the adjustable angle piece to fulfill the second. We will report on the final design and will have a sample to demonstrate.

WP-23 The MotOrtose project - development of a motorized upper extremity orthosis for ALS

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Keywords: clinical care, support

Background: Regardless of MND subtype, early loss of arm function constitutes a major challenge to the maintenance of activities of daily living as well as quality of life.

Care includes a multidisciplinary team which provides technical aids tailored to the loss of function experienced by the patient. Whereas loss of lower extremity function is substituted with electric wheelchairs securing mobilization, the availability of aids to substitute upper extremity function is limited.

In collaboration between the Department of Mechanical and Industrial Engineering, Norwegian University of Science and Technology, and the Department of neurology at St Olav's University Hospital, a prototype of a motorized combined elbow and shoulder orthosis has been developed. At project initiation, the project goal was to make a motorized exoskeleton with a range of movement sufficient to move a paralysed arm from a vertical downward position up to the face. The total weight should be reduced to an absolute minimum.

A prototype was finished in 2018 meeting the project goals. Movement is secured by two actuators localized on the upper arm orthosis. Sufficient weight distribution was obtained by means of a carbon fibre torso exoskeleton. The control mechanism was originally manual, but due to paresis of the other arm, a pedal with two rods is now in use. At present, we are developing new prototype along to axis. We investigate alternative mode of actuator engagement, including voice control. We hope to achieve pronation/supination control in the next version.

We will provide pictures and a video demonstration of the prototype orthosis.

WP-24 High-throughput screening for the development of novel ALS treatments

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Keywords: screening tool, drug target

Background: High-throughput cell-based phenotypic screens are one of the golden standards in drug discovery. Such screens enable the testing of large chemical compound libraries in a rapid and efficient manner. Using this approach, the Genomic Instability group, led by Prof. Fernández-Capetillo at the CNIO in Madrid (Spain), successfully developed an ATR kinase inhibitor with potent anti-cancer activity (1). Building on this success, Prof. Fernández-Capetillo has recently started a second lab, located at the Karolinska Institutet in Stockholm (Sweden), which focusses on the use of cell based high-throughput phenotypic screens to discover and explore novel treatments for rare diseases, such as ALS and Huntington's Disease (HD).

To this end, we have established different cell models mirroring some of the pathological phenotypes occurring in ALS, such as cell death due to TDP-43 aggregation or the di-peptide repeats resulting from the intronic hexanucleotide repeat expansion in C9ORF72. In addition, we are currently developing a cellular model of HD in which Huntington containing a poly-Q repeat expansion is expressed. Finally, we are not only working with cellular models, but also with higher vertebrate models such as zebrafish, for which we are developing inducible ALS and HD systems for high-throughput screening. Taking advantage of our group's expertise in high-content microscopy screens, we are also testing different chemical libraries in the search for compounds that are able to target undruggable proteins related to ALS onset.

Our lab is located at the Science for Life Laboratories, which houses many national facilities, amongst them the Laboratories for Chemical Biology at Karolinska Institutet (LCBKI), which grants us access to up to 200,000 compound libraries, ranging from FDA approved drugs, tool compounds with known target, to uncharacterised and chemically diverse libraries. Using one of these chemical collections (4,126

compounds), we have recently identified compounds that can limit the toxicity of the ALS-related PR20 di-peptide (2). In a different context, we have also discovered compounds that are capable of inducing the expression of the immune-checkpoint ligand PD-L1 in a subset of breast tumors, highlighting the robustness of our strategy as well as the broad-spectrum of applications in which it can be applied. Our general strategy for the discovery of novel ALS and HD therapies will be discussed.

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Care practice**CP-01 Challenges and success of rowing across the Atlantic by an individual with ALS**

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Keywords: QoL, exercise, adaptations

Background: The Talisker™ Whisky Atlantic Challenge is the premiere ocean rowing event, requiring 3000 miles of rowing across the Atlantic Ocean, from the Azores to Antigua, with no external support. The challenge is difficult for all who attempt (30 teams/year) and physical demands are extreme. The pace is grueling with 2 hours of rowing and 2 hours of sleep, repeated for 35-60 days. When an individual with Amyotrophic Lateral Sclerosis (ALS) desires to row across the Atlantic there are extra challenges and successes!

Objectives: We will describe the events before, during, and after the row across the Atlantic.

Methods: Case: AA is a 57 year old male (175.3 cm, 75 kilograms), with upper motor neuron predominant ALS (El Escorial probable), diagnosed 18 years ago. Primary issues are dysarthric speech and spastic gait (use of walker at home and power wheelchair outside) with ALS Functional Rating Scale-Revised (ALSFRS-R) of 36; slow progression with symptoms stable for 6 years. He began his training 18 months prior to the race using a rowing machine program 30-45 minutes 4-5 days per week and 1 day for 60-90 minutes, and an additional 3 days of weight training per week. Diet focused on increased protein for increased weight gain. Weight before trip was 89 kg.

Results: Challenges: The boat was 28 feet long and 70 inches wide, with a cabin at each end. The space was limited and required quick movements in and out of cabin door to prevent water entering. The deck was always wet and the boat was in constant motion. There was a need to learn to don the emergency suit quickly if needed. The rowing seat required adjustment to account for decreased range of motion in hips from spasticity. There was a need to adjust for standard rowing shifts because of fatigue (both mental and physical).

Solutions: A 5 person rowing team was established; a custom rowing seat was built; a stretching exercise program was established throughout the 18 months and modified while on-board; a rowing schedule was modified to facilitate better efficiency of the team and longer periods of rest for AA.

Success: The team made it in 51 days, 11 hours, 57 minutes. The team rowed 3548 miles. AA became the first person with ALS to successfully row across an ocean.

Discussion and conclusions: For many individuals with ALS purpose and quality of life include fulfilling dreams even when the dreams require extreme physical and psychological demands. AA demonstrates that even a disease characterized by progression of physical decline and degeneration does not have to limit goals in life.

CP-02 ALS and full-marathon: Response to edaravone treatment

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Keywords: edaravone, therapy, full-marathon

Background: Excessive physical exercise including full marathon may be a risk factor for developing ALS (1). In full marathon, motor neurons throughout spinal cord must keep firing for more than 3 hours to complete 42.195 km running. This might cause oxidative stress in motor neurons, leading to the possibility to the onset of motor neuron disease. Free radical scavenger edaravone (2), thus might rescue motor neurons in such patients.

Objectives: We experienced 4 patients with ALS whose habits are full marathon and initiated edaravone treatment.

Methods: Patient 1: Forty-nine year old male noticed bilateral shoulder muscle weakness in January 2017. Three months later his full-marathon score was 1 hour behind his best score. He was diagnosed to have laboratory-supported ALS in April 2017 and started both edaravone and riluzole treatment. His disease progression was rapid. He lost bilateral arm function in January 2018 and needed almost 24 hour BiPAP and lost walking ability in January 2019.

Patient 2: Fifty-nine year old male developed dysphagia in April 2017. His full-marathon score in October in 2017 was worst for him. He was diagnosed to have definite ALS in May 2018 and both edaravone and riluzole treatment were initiated. His ALSFRS-R score decreased from 43 to 36 during 1 year.

Patient 3: Forty-eight year old male noticed weakness of left hand in January 2018. The weakness spread to left arm and he felt spasticity subsequently. Eight months later he was diagnosed to have probable ALS and both edaravone and riluzole treatments were initiated when his ALSFRS-R score was 46. He joined a half marathon race 4 months later, and the time was almost the same as before. Seven months later although his grip strength slightly diminished, his ALSFRS-R score was unchanged.

Patient 4: Fifty-six year old male noticed slight spasticity of right leg in December 2018, when his full marathon time was 45 minutes behind his best score. His grip strength also diminished and diagnosed to have probable ALS 3 months later. He started both edaravone and riluzole treatment. After the treatments, fasciculation of both arms almost disappeared and he does not feel spasticity when he jogs.

Results: Among 4 ALS patients who run full marathon, one patient deteriorated rapidly but in the other 3 patients the disease progression was milder.

Discussion and conclusions: About 0.26% of Japanese population enjoyed full-marathon race in 2017. Among 79 ALS patients who visited the clinic in 2017 to June 2019, 4 patients (5.1%) are full-marathon runners, suggesting that full-marathon might be a risk factor. Although the observation period is short, the earlier initiation of edaravone might be beneficial for ALS patients who have excessive physical exercise including full-marathon.

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CP-03 A pilot project to determine if standard ayurvedic treatment protocol alters the progression of ALS

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Keywords: disease progression, ARREST, Ayurvedic treatment measures

Background: Incidence of ALS shows increasing trend in developing countries like India. Patients are unable to afford treatment modalities. Low cost and patient's friendly treatment modalities will be effective. At present, there is no specific treatment for any of the motor neuron diseases, otherwise only supporting measures are possible. None of the known modalities arrests the progression of the grave disease. This pilot project will investigate an *Ayurvedic* treatment protocol and its potential impact on the progression of MND.

Objectives: The aim was to streamline and standardise the *Ayurvedic* treatment protocol for the management of MND via these objectives:

- To assess the prevalence of MND in Thrissur district of India through survey
- To improve the quality of life of MND patients
- To more effectively manage MND and evaluate the impact on progression of the disease
- To evolve a database for further research in degenerative disorders of nervous systems
- To render cost effective and patient friendly pharmaceutical Ayurvedic formulations and treatment
- To give training and awareness programs to doctors and public.

Methods: A comprehensive approach by incorporating *Ayurvedic* treatment principles like *Pachana, Deepana, Anulomana, Rookshana, Snehana, Sweda, Sodhana, Samana and Rasayana* along with physiotherapy, yoga and psychiatric care is the mode of operation followed in this project. *Ayurvedic* treatment includes external therapies (oil massage, powder massage, enema etc.) and internal therapies (decoction, medical oil, oral applications etc) to manage the signs and symptoms. 67 patients were offered ayurvedic treatment measures for a period of 1 month.

Results: Norris ALS scale and the Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFERS) were used for assessing the functional status/quality of life of MND patients. Among 52 MND patients, 46% of patients had an improvement in Quality of life, 19% of patients got worse and 35% of patients had no change in Quality of life after the course of *ayurvedic* treatments.

Discussion and conclusions: This pilot project is underway in government Ayurveda hospital under national Ayush mission. In this preliminary work, some parameters like tone of muscle, dysarthria and quality of life show positive response. By doing powder massage tonicity were found to be increased in ALS patients, by applying the *lepanam* (tongue application) found to effective in dysarthria and quality of life (QOL) of patients found to be more effective in ALS than bulbar origin type of MND.

Acknowledgements: We would like to thank patients for taking part in this study. National Ayush mission provided funding for this study.

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CP-04 A systematic review of diet and exercise clinical trials among people with amyotrophic lateral sclerosis

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Keywords: diet, exercise, review

Background: The complexity and heterogeneity of ALS present a significant challenge to developing successful treatment options (1). Without a cure, the aims of patient care focus on symptomatic management to improve quality of life (QoL) and extend the survival of patients. There is emerging interest and research in physiotherapy and dietetics to explore exercise and nutrition interventions and to determine their potential disease-modifying effects in people with ALS (2). Some evidence has concluded that aerobic and resistance exercise is associated with improved patient muscle function and QoL (3). Additionally, research of nutrition interventions has described the potential benefit of diet modifications and supplements on survival, due to their anti-inflammatory and neuroprotective properties (4). However, there is a lack of rigorous clinical research in both fields from which to draw firm conclusions.

Objectives: To systematically review and synthesize findings from clinical trials of exercise and nutrition interventions for people with ALS.

Methods: We searched MEDLINE, EMBASE, CINAHL, CENTRAL and Scopus from inception to April 2019 for interventional studies examining the effects of exercise and/or nutrition interventions in people with ALS. The quality of the included studies will be assessed by two independent reviewers using the Physiotherapy Evidence Database (PEDro) scale. Complementary criterion will be incorporated from the Quality Criteria Checklist obtained from the American Dietetic Association Evidence Analysis Manual.

Results: Our literature search identified 4584 studies, and three articles were identified through hand-search. After removing duplicate citations, 2948 studies underwent title and abstract screening. Of those, 100 were considered potentially

eligible and after full-text screening, 38 studies met the inclusion criteria; 16 conducted an exercise intervention and 22 conducted a nutrition intervention. These eligible trials will undergo quality assessment and data extraction. The key characteristics of the included papers will be presented.

Discussion and conclusions: This systematic review will present and synthesize all clinical evidence on exercise and nutrition interventions in people with ALS. It will identify effective treatment options and assist multidisciplinary teams to better support people with ALS. Additionally, this review will identify current gaps in the literature and thus, inform the direction for future research.

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CP-05 Supporting choice in dysphagia management through naturally thick drinks

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Keywords: dysphagia, disease burden,

Background: Dysphagia for liquids is a frequently reported symptom in people with Motor Neurone Disease (pwMND). A Speech and Language Therapy (SLT)

recommendation for thickened fluid is a common dysphagia management strategy. Thick drinks can help to reduce the occurrence of aspiration and reduce the volume of loss from the mouth for pwMND who have poor lip seal. Preparing thick drinks typically involves mixing a prescribed number of scoops of a commercial thickening powder into a stated volume of liquid. These powders are convenient with clear preparation guidelines however, many pwMND find these drinks unpalatable or report an aversion to drinking a texture that does not have a 'normal' mouth feel. This can lead to choices to continue thin drinks despite uncomfortable aspiration and/or possible dehydration secondary to reduced fluid intake.

Objectives: The aim of this project was to offer pwMND increased choice, autonomy and a sense of normality by supporting them to prepare safer drinks with everyday ingredients.

Methods: As a joint quality improvement initiative, the SLT departments in Beaumont Hospital, Dublin and the local primary care team of North Dublin developed a booklet on preparing naturally thick drinks. We used a plan-do-study-act approach. We researched existing resources, tried out recipes and rated drinks according to thickness as per our Irish national consistency descriptors. We extended our scope to include basic information on the swallow process, hydration and suggestions of naturally thick shop-bought items.

Results: We produced and piloted a draft A5 booklet. The pilot was audited through written feedback from service users, their relatives and various healthcare professionals. We reviewed and applied this feedback creating our final booklet. This booklet is now routinely provided to suitable pwMND.

In the recipe section, the fluid grade is stated for the drink as described in the recipe as well as tips to thin or thicken drinks to modify them for other fluid grades.

Discussion and conclusions: Suitable service users require a retained understanding of the nature of their dysphagia and the benefit of consuming thick rather than thin drinks. They or an identified care partner must be physically and cognitively able to prepare their own drinks by following the recipes and to judge if the drink they prepare correlates to their recommended grade of fluid thickness.

This fifty page recipe booklet has been very well received by pwMND experiencing dysphagia. From an SLT perspective, we have an additional resource to present when recommending thickened fluid to support autonomy and choice making for people who do not wish to just use a commercial thickening powder. Relating the thickness of the recommended fluid grade to everyday drinks also helps pwMND translate SLT advice into their own personal daily management strategy.

CP-06 The impact of gastrointestinal related symptoms on nutrition intake - the role of the dietitian in managing gastrointestinal complications in persons living with MND

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Keywords: nutrition, appetite, gastrointestinal symptoms

Background: Malnutrition is a negative prognostic factor of survival in persons living with MND (PlwMND). The severity of gastrointestinal (GI) symptoms and impact this has on PlwMND is often underestimated.

In our practice patients often complain of GI symptoms. These can range from early satiety, diarrhoea, constipation, bloating,

reflux and overall abdominal discomfort. These GI symptoms can have a negative impact on a person's intake, overall nutritional status and day to day activities.

Management of these symptoms can be quite complex, challenging, and often management is not a 'one size fits all' approach. The insertion of a gastrostomy tube and the implementation of NIV may also add another layer of complexity but can also be useful in alleviating these symptoms.

Objectives: To highlight the common GI issues in PLwMND. To highlight the impact GI symptoms on nutrition status. To highlight the important role of the dietitian in the management of GI symptoms. To demonstrate the effectiveness of MDT in managing symptoms.

Methods: A literature review was conducted to: 1. Demonstrate and review the prevalence and common GI issues affecting patients with MND; 2. Obtain current evidence based practice in the management of GI symptoms in cohort. Observations and experiences in our day to day clinical practice will also be reported on.

Discussion and conclusions: Through our clinical practice we have found the reporting and management of GI symptoms is varied and multifaceted in our MND patients. GI symptoms can have a profound effect on appetite and intake and overall nutritional status which can lead to poor outcomes.

Dieticians have an integral role in:

- identifying issues that impact on optimal intake which include exploring GI symptoms
- providing individualised management to target these issues
- providing support and monitoring throughout the disease process

Anecdotally, this support and management may assist to not only improve nutrition outcomes but also overall comfort, wellbeing and quality of life. Management of

these issues requires a multidisciplinary approach including input from Medical, Nursing, Pharmacy and other Allied Health.

Further studies to focus on QoL, determining staging of symptoms and effectiveness of interventions need to be conducted. In addition, the relationship between diet and the microbiome in PlwMND and the targeted dietary interventions requires exploration.

Acknowledgements: We would like to thank the remarkable patients and carers who have opened up to us throughout their journey with MND and the dedicated team at Calvary Health Care Bethlehem.

CP-07 Developing a web-based patient decision aid for gastrostomy in MND: the DiAMoND study

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Keywords: decision making, multidisciplinary care, gastrostomy

Background: Due to the multisystem effects of MND, patients are faced with many complex healthcare decisions, one of which is whether to accept gastrostomy feeding. The evidence base for the benefits of enteral feeding in MND is lacking (1), meaning this decision is not straightforward for patients. In the UK, there are currently no published decision aids (DAs) to support patients making this decision.

Objectives: This study will develop and pilot a web-based DA to: provide evidence-based information on gastrostomy placement, management and feeding; communicate the risks and benefits associated with each option; check understanding; and clarify personal values and preferences, enabling patients to make decisions congruent with their values and appropriate for them.

Methods: A two-phase process will be used to develop the DA, over 24 months from January 2019. The methods are based on a validated model for web-based DAs (2) and the International Patient Decision Aid Standards (3), and will observe the Medical Research Council's guidance for the development of complex interventions (4). Phase 1 will use literature reviews and stakeholder interviews to identify essential content for the DA and explore the best way to present this. Once the necessary content has been identified, a systematic search of the evidence will be conducted for each piece of information, to ensure scientific accuracy.

In the second phase, a prototype DA will be developed using the results of Phase 1, and revised in an iterative process, using stakeholder feedback and discussions with

the study advisory committee. Stakeholders will include individuals with MND, their carers and the healthcare professionals (HCPs) working with them. People with MND will be broadly representative of the UK MND population in terms of age, gender and subtype of MND, and will include both people who currently live alone and people who live with others. HCPs will be drawn from a variety of disciplines including doctors, nurses and allied health professionals.

Results: Following development, a feasibility study will explore the acceptability, practicality and usefulness of the DA for patients, carers and HCPs in clinical practice, and the DA will be refined from this feedback. On completion, the DA will be widely disseminated to the MND community through a launch event, research publications and presentations, stakeholder websites and social media.

Discussion and conclusions: This process aims to embed the DA in clinical practice, to ultimately improve the decision-making process and quality of decisions for people with MND.

Acknowledgements: Jointly funded by Marie Curie Research Grant (MCRGS-20171219-8005) and Motor Neurone Disease Association (963-794)

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CP-08 The effect of feeding tube placement on body mass index and Amyotrophic Lateral Sclerosis Functional Rating Scale Revised

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Keywords: gastrostomy, BMI

Background: Low body mass index (BMI) has been shown to be a significant predictor of shortened survival in patients with amyotrophic lateral sclerosis (pALS) (1). Additionally, weight loss has been shown to be strongly associated with shorter survival in pALS (2). Multiple factors contribute to weight loss, including dysphagia, hypermetabolism, fatigue, self-feeding difficulties, and depression. Traditionally, a feeding tube is offered when pALS experience weight loss, have difficulty swallowing, or with a decline in vital capacity. Anecdotally, feeding tubes can help improve quality of life; however, to date, no studies have been found that examine the quantitative clinical benefits of feeding tube placement. This study set out to determine if feeding tube placement has an effect on pALS BMI or their rate of decline, shown by the ALS Functional Rating Scale Revised (ALSFERS-R).

Objectives: To determine if feeding tube placement in the ALS population has a positive effect on rate of change for both BMI and ALSFERS-R.

Methods: The population reviewed consisted of patients in an academic hospital's interdisciplinary outpatient ALS clinic in the United States. BMI and ALSFERS-R were measured and documented at diagnosis date and at clinic visits following diagnosis. Patients that had a feeding tube placed during their illness

were enrolled in the data review. The review consisted of 50 patients with subset analysis performed for gender and location of disease onset. Rate of change for BMI and ALSFERS-R were calculated.

Results: Data analysis continues, with the aim of determining if feeding tube placement has an effect on BMI and rate of decline for ALSFERS-R. Subset analysis will provide insight on whether feeding tube placement has direct benefit for specific gender and location of disease onset.

Discussion and conclusions: This review highlights that more research is needed to determine the clinical benefits of feeding tube placement with respect to BMI and ALSFERS-R. This study is limited due to the small sample size and limited number of clinical visits for some pALS prior to and after feeding tube placement. As is noted in current ALS research, BMI and weight loss have an influential role in accelerating the progression of disease. Further research needs to be undertaken to determine if feeding tube placement should be more prominent in the discussion of factors that can ameliorate the course of the disease.

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CP-09 Oscillating PeP (O-PeP) devices versus Expiratory Muscle Trainers (EMTs) for lung recruitment in ALS patients prior to NIV

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Keywords: respiratory function, respiratory care

Background: Lung recruitment is the practice of increasing airway pressure with a goal to open collapsed alveoli and keep the lungs open. The goal of recruitment is to serve as part of a lung protection strategy; making it easier to cough and breath.

O-PeP and EMT devices apply positive expiratory pressure (PEP) as the patient breathes through a mouthpiece. Breathing out harder against the resistance opens airways, creates PEP which holds airways open, and aids in recruitment of alveoli. O-PeP devices use oscillation while also creating PEP. EMT devices do not use oscillation but do also create PEP. The use of EMT has been shown to slow the decline of Maximum expiratory pressure (MEP) and keep patients above predicted baselines longer (1). Lung recruitment has also been shown to aid in dysphagia, and increase peak cough flows (2).

Objectives: We seek to compare O-PeP devices and expiratory muscle training devices when used as recruitment agents. The aim is to gauge the effectiveness, ease of use and proper scripting for the devices as recruitment pre-NIV tools.

Methods: Patients will use device(s) as instructed (O-PeP and/or EMT). Patients enrolled will have FVC ranging between 60-80%. Patients will be instructed on the frequency of use (between 35-70 times daily), with FVC, MIP and MEP measured every 3 months. The frequency of use will be recorded at each visit using a self-report from the patient.

Group 1 – O-PeP device alone
 Group 2 – EMT device alone
 Group 3 – O-Pep and EMT device together
 Group 4 – Control group*

* The control group will consist of patient who declined to participate in the study but agree to continued monitoring of their progress.

The data will be analyzed by looking at the percent change of the measured data then seeing if there are any trends across the different groups.

Discussion and conclusions: Is O-PeP more effective in recruitment then EMT? Are they the same or does one work better at 60% or 80%? If they are used as adjuncts, what is the best frequency to be used? Will targeting recruitment keep the FVC and corresponding respiratory measurements level as long as they out pace the rate of decline? Can the devices be used to prolong “off NIV time” and keep patients breathing comfortably?

We expect that O-PeP devices will be more effective, and patients with a higher FVC will see greater results from the interventions. We also expect to see the patients with a higher frequency of use will see better results.

Acknowledgements: MDA ALS Center of Hope

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CP-10 Pneumothorax in neuromuscular disease associated with lung volume recruitment and mechanical insufflation-exsufflation

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Keywords: lung volume recruitment, respiratory care, pneumothorax

Background: Lung volume recruitment (LVR) and mechanical insufflation-exsufflation (MI-E) are techniques that deliver positive pressure via a facemask or mouthpiece to hyperinflate the lungs until maximal assisted lung insufflation capacity is reached. These methods improve cough and inspired lung volume, and are recommended when airway clearance is necessary or during episodes of respiratory tract infection. Guidelines for the respiratory management of people living with MND and other neuromuscular diseases typically advocate the use of LVR and/or MI-E as part of a daily preventative management strategy to maintain lung function and avoid infections, although the evidence base for these recommendations is poor. We present a review of the literature and two case studies of pneumothorax associated with LVR or MI-E; one in a person with MND, to highlight this rare but serious adverse event.

Case 1: A 71-year-old male with MND presented to the emergency department with worsening dyspnoea and chest pain immediately following LVR therapy. Chest radiograph revealed a large right-sided pneumothorax.

Case 2: A 25-year-old male with Duchenne muscular dystrophy presented to the emergency department with chest pain and dyspnoea secondary to a large right-sided pneumothorax. Onset of symptoms began following prolonged use of mouthpiece intermittent positive pressure ventilation and multiple sessions of MI-E.

Literature Review: The prevalence of people with MND or other neuromuscular diseases who are on home mechanical ventilation is conservatively estimated at 3 people per 100,000. Within this small population very few cases of pneumothorax have been published, and there are no published data identifying lung function thresholds or respiratory system compliance values that have been associated with an

increased risk of pneumothorax when LVR and/or MI-E are used.

Discussion: It is unlikely that robust measures for risk of pneumothorax can be developed and prospectively validated for such an apparently rare complication. As such, clinicians must decide whether therapy is justified based on the patient's current presentation, primary pathology, comorbidities, likely disease trajectory, aim of LVR or MI-E therapy and ability to perform the techniques safely. The presence of prior pathology is a precaution that warrants careful consideration when prescribing LVR or MI-E. Where no established risk factors exist, clinicians should still consider the goals of therapy and discuss the risks versus benefits with users.

CP-11 Long-term follow-up for patients undergoing presymptomatic genetic testing for C9orf72 and SOD1

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Keywords: genetic counselling, pre-symptomatic, follow-up

Background: Approximately 10% of amyotrophic lateral sclerosis is familial (FALS), and for about ~50% to 70% of those with familial disease a pathogenic variant in an identified FALS gene can be found. For individuals in these families, presymptomatic testing is an option. Guidelines for presymptomatic pre- and post-test genetic counseling exist and have been updated as additional genetic loci have been identified; these guidelines have been based in part on experience with Huntington disease (HD) and other late-onset neurodegenerative disorders. Post-test genetic counseling is typically limited to a single session; resources are provided

including support groups and patient foundations, if available. Long-term follow-up to minimize any potential adverse effects of learning the results (positive or negative) should be in place, but the structure, recommendations, and patient needs for this type of follow-up care are not as well-studied.

Objectives: This study looked at the long-term effects of receiving both positive and negative FALS presymptomatic testing results, as well as the patients' perception of the effectiveness of the modified FALS counseling protocol.

Methods: The participant sample for this study comprised 20 participants seen in Northwestern Medicine's Neurogenetic Counseling Clinic for presymptomatic genetic counseling and testing for known familial variants in either SOD1 or C9orf72 from October 2017 to May 2019. Study is ongoing, and interested participants complete a survey and can opt in to participating in a semi-structured phone interview for which prominent themes will be identified and rated.

Results: As of the writing of this abstract, five participants responded to the survey and have opted in for the requested interview; these interviews are scheduled for July. This participant group includes C9orf72-positive, SOD1-positive, C9orf72-negative, and SOD1-negative individuals. Participants were asked about various aspects of their experiences including stress levels and emotional states currently and at various points post-disclosure. Participants will be prompted to discuss examples of helpful aspects of the counseling sessions, recommendations for modifications, and discussed the impact of the test results on their lives since disclosure.

Discussion and conclusions: This study is based on participants who have undergone presymptomatic FALS testing following the recommended modified HD-like protocol, which provides an educational and supportive environment for this

potentially psychologically distressing process. This study will give insight into the patients' experience and allow for adaptations to improve and/or plan for the process and long-term psychological outcome, as well as learn how the results impact subsequent life decisions like family, financial, and/or career planning.

Acknowledgements: I would like to thank the patients for taking part in the study.

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CP-12 Familial amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD): Identifying the need for a new genetic counselling model of care

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Keywords: genetic counselling, genetic testing, FALS

Background: Genetic counsellors are advocates and educators. The role of genetic counsellors includes facilitating the integration of genetics and genomics into other healthcare disciplines. According to recent recommendations, genetic testing should be offered to all individuals affected with Amyotrophic Lateral Sclerosis (ALS) or

frontotemporal dementia (FTD), but there are no consistent approaches nor consensus guidelines. Genetic testing of affected patients, when offered, frequently occurs within a multidisciplinary neurologist-led clinic, often without the involvement of a genetic counsellor. Once a pathogenic variant is detected, biological relatives should be offered genetic counselling within the clinical genetics setting and may choose to undergo predictive or reproductive genetic testing.

Objectives: To highlight the complex genetic counselling issues that can arise in genetic testing for ALS and FTD genes, and propose the need for a client-centred model of care.

Methods: We present three illustrative case studies that highlight patients and families' varied experiences of genetic counselling and testing for familial ALS/FTD in Australia.

Results: Case 1 highlights that genetic testing can be appropriately conducted outside of a clinical genetics unit, but challenging cases benefit from genetic counsellor input. Case 2 demonstrates the varied responses of health professionals to ALS/FTD genetic testing and the need for further education about the complexities of genetic testing decision-making. Case 3 highlights that inconsistent results between laboratories can occur (particularly in C9orf72 expansion testing) and therefore the limitations of our current knowledge should be discussed pre-test to ensure informed decision-making.

Discussion and conclusions: These cases demonstrate that complex issues frequently arise in familial ALS and FTD, and in some cases, adequate care for patients or at-risk relatives is lacking. In order for genetic testing and counselling practice to be integrated into neurology, specialist health professionals require additional education and support to identify and manage the challenging issues that can arise. In addition, recent guidelines for care

of the ALS or FTD patient do not include genetic testing or are out of date. To better meet the needs of patients with ALS or FTD, along with their families and health providers, we are conducting a research study aimed at developing a new model of genetic counselling in mainstream neurology care. The goal of this new model will be to provide patients and families with consistent, evidence-based care that facilitates informed decision-making, and promotes adjustment to a diagnosis of familial ALS and FTD.

CP-13 Differentiating needs of informal caregivers of ALS patients across the caregiving course: a systematic review

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Keywords: caregiver, support, needs

Background: Informal caregivers of patients with amyotrophic lateral sclerosis (ALS) experience a range of needs across the course of the disease. For the provision of adequate support, an examination of the empirical evidence is necessary.

Objectives: The purpose of the systematic review was to synthesize evidence of needs of informal caregivers of people with ALS at different stages of caregiving.

Methods: We conducted a systematic review of empirical research on needs of ALS informal caregivers in both English and German from 2000 to August 2018. We searched the databases EMBASE, MEDLINE (PubMed), PsycINFO and CINAHL for relevant entries. Study selection

and data extraction was done independently. Both quantitative and qualitative studies were included. We used the Joanna-Briggs-Institute checklist for quality assessment of qualitative studies and an adapted version of the NIH checklist for quantitative observational studies. Caregivers' needs in these stages were initially sorted into categories of informational, practical, physical, psychological, emotional, and social needs within the supportive care framework (1). These categories of needs were then used to guide narrative synthesis (2). We linked the narrative synthesis of study results to five stages of caregiving: 0. journey to diagnosis, 1. early coping and adjustment after diagnosis, 2. maintenance, 3. transition to end stage, and 4. coping with change and loss (3).

Results: We included 42 full-text articles in data extraction. Our preliminary data analysis indicates that needs differ across the five caregiving stages. While the first stages 0. and 1. include primarily informational and emotional needs, the period 2. between diagnosis and transition to end-of-life care includes a vast array of needs. The transition to end stage 3. entails primarily needs in relation to palliative care provision, as well as emotional needs. There is scarce research on needs relating to bereavement 4. of informal caregivers of patients with ALS.

Discussion and conclusions: Many studies do not differentiate by caregiving stage explicitly. Healthcare professionals should pay attention to current caregiving stages and possible arising needs for the caregivers. Further research is needed for the time between diagnosis and end-of-life care as well as for the bereavement phase.

Acknowledgements: We thank Miriam Galvin for her initial feedback on the review protocol and Hannah Ewaldt for her consult on the search strategy. This study is funded by the Swiss Academy of Medical Sciences.

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CP-14 Family caregivers in ALS and their vital need for self care

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Keywords: caregiver, QoL, supportive care

Background: Informal palliative care at home is distinguished from professional care by a different process. Professionals are skilled in detachment strategies, they care for several people. When I accompany my child, parent, sibling, lifetime partner or spouse, this is unique, and I give my love in particular. It is a process that you grow into, not a process of disidentification or inner distancing, but of distance regulation with an 'as well as'. Out of love, I pay my attention and at the same time I have to respect my own limits. So I am responsible for both a seriously ill increasingly physically disabled person and my own boundaries. If I decide to assist a beloved person during the progression of an irreversible illness, this is only possible if I regulate my resources and thus my own energy balance can remain stable. This contribution is motivated by personal experience as a former informal caregiver of a person with ALS.

Objectives: Explore strategies for self care by family caregivers in ALS and facilitate peer sharing.

Methods: Small sample of short open-ended interviews with family caregivers in ALS in Switzerland and the Netherlands.

Results: Work in progress

Discussion and conclusions: Caring relatives are responsible not only for care but also for self-care. It needs an adequate demarcation. I draw a line by being either entirely with my partner or myself. It helps to live in the present (1). If you have the finiteness of life in mind, then the focus is on the essence, on what is really important, and you live differently: in the now. When sad, we know what is at stake, which in turn allows for intensity in life. Being able to experience the simplest in everyday life and the unspectacular intensively together gives strength for the moments of desperation, overburdening and crisis situations that can occur again and again, but for which you have prepared beforehand as far as possible. One is more careful with the other person and with oneself. Just as helpful in caring for oneself is when caring relatives are certain of their self-efficacy (2). If I remain in charge of the situation, I can work on solutions and stay attentive. I can grow in sorrow and find meaning in life despite grief. You reach your limits and grow beyond borders.

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CP-15 Group interventions for ALS caregivers: A randomised controlled trial protocol

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Keywords: caregiver, therapy, clinical psychology

Background: ALS is a multidimensional condition, with many patients presenting with cognitive and/or behavioural impairment. Caregivers of patients with ALS, commonly non-paid immediate family members, often take primary responsibility for the complex care needs of patients in non-medicalised setting, and many as a consequence experience caregiver burden, anxiety, and/or depression.

Objectives: With a goal of developing improved clinical service for ALS caregivers, we aim to determine which intervention, if any, within a 6 to 8 week framework leads to a reduction in psychological distress. In doing so, we aim: 1) to evaluate the effectiveness, efficacy and feasibility of low intensity interventions for mild-to-moderate anxiety, depression and burden in caregivers of ALS patients using a cohort of Irish ALS caregivers; 2) to inform best practice regarding the mental health needs of caregivers of patients with ALS both nationally, and internationally; 3) to evaluate what ALS-specific patient factors predict caregiver outcomes regarding the efficacy and effectiveness of intervention programmes; 4) to identify a standard intervention programme suitable for ALS caregivers, which in turn will define a clinic-based pathway for future enrolment to such an intervention.

Methods: This randomised controlled trial (RCT) will use randomisation to allocate participants into three parallel groups with a 1:1 ratio. The RCT consists of two intervention groups and a waiting-list treatment as usual (TAU) group. The intervention arms of the trial consist of a 'Mindfulness-based Stress Reduction' and 'Building Better Caregivers' manualised group-based intervention. The TAU group will have access to intervention at the end of

the trial period. Primary outcomes are self-report questionnaires on anxiety and depression symptoms, with caregiver burden and quality of life considered secondary outcomes. Assessment will commence at baseline, immediately following the intervention period, and after a period of 12 weeks to assess the effectiveness and efficacy of participating in an intervention. Patient cognitive and behavioural data will also be considered as a mediating factor.

Discussion and conclusions: This RCT will test the efficacy and effectiveness of group-based interventions compared to each other, and to a waiting list cohort representing treatment as usual. This study will provide information on how an intervention may meet the needs of participants and will inform future practice and research.

Acknowledgements: This project has been funded by the ALS Association (ALSA).

CP-16 Interventions targeting the psychological well-being of carers of people with motor neurone disease (MND): a systematic review

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Keywords: caregiver, QoL, well-being

Background: The significant psychological toll of caring for a person with MND is well-established and includes significant caregiver burden, depression and anxiety, as well as poor quality of life. There is increasing recognition that the psychological well-being of MND carers needs to be

addressed and the interest in interventions directly focussing on MND carers is increasing.

Objectives: The objectives of the review were to: a) summarise the interventions designed to improve the psychological well-being of carers of people with MND; b) assess the quality of the evidence regarding interventions designed to improve the psychological well-being of carers of people with MND; and c) evaluate the effectiveness of any intervention designed to improve the psychological well-being of the carers of people with MND.

Methods: The design of the systematic review followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and the protocol was registered with PROSPERO. The search included 12 databases of both published and unpublished intervention studies. The review considered studies that were quantitative or qualitative in nature or both (mixed methods) as long as the quantitative or qualitative component could be extracted separately. To be considered for inclusion, study interventions had to include any form of intervention delivered in any combination, modality, duration or dose targeting the psychological well-being of carers of people with MND. Studies targeting spousal, family and informal carers were included whilst professional or paid carers from government or private providers were excluded. The review included carers of people with MND independent of disease stage (e.g. mild, moderate, severe, palliative, recently deceased) and care setting (e.g. home, hospital, residential care, palliative care). Comparators included no intervention, other nonpharmacological interventions or usual care (controls). Studies with one group were also accepted. The primary outcome of interest had to be an outcome related to the psychological well-being of carers inclusive of any psychologically related outcome (e.g. burden, quality of life, anxiety, depression). Joanna Briggs Institute (JBI) screening

protocols and standardised critical appraisal instruments were used by three independent reviewers to assess inclusion and methodological quality.

Results: Nine papers were identified covering a variety of interventions including dignity, mindfulness, spiritual therapies and case management. The number of participants ranged from 13 to 126. Most studies were of poor methodological quality. The designs were also varied and included repeated measures with or without a control group, randomised controlled trials and longitudinal survey approaches. Significant benefits were uncommon amongst studies using quantitative outcomes, whilst some qualitative data were supportive.

Discussion and conclusions: Initial findings indicate that there is not any current strong evidence to support the use of any one specific intervention type. Future research should focus on improving the methodological quality of studies, consider tailoring and the application of theory to intervention design.

CP-17 Efficacy of a group-based mindfulness program for people with motor neurone disease and their family caregivers

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Keywords: clinical care, coping, mindfulness intervention

Background: The average life expectancy of people with motor neurone disease (pwMND) is 2.5 years, with many experiencing stressful delays before formal

diagnosis. In the time following diagnosis, pwMND and their family members (fmMND) face significant psychological adjustment in response to increasing disability and anticipation of a shortened lifespan. Many pwMND and family members consequently experience significantly lowered quality of life and increased rates of psychological illness. Despite this, there has been extremely limited investigation of psychological interventions that address their specific needs. Mindfulness-based interventions appear promising in this area, with recent research demonstrating decreases in distress and reduced psychological illness across a wide range of health conditions, including MND.

Objectives: Our ongoing study explores the feasibility and efficacy of a group mindfulness program that has been designed to be sensitive to both the shared and separate needs of pwMND and their fmMND caregivers in an Australian context.

Methods: Consent to a group mindfulness program is being sought from eligible patient-caregiver dyads attending a specialist multidisciplinary MND clinic. The program involves 4 sessions and a follow-up, over a 10 week period. To examine the effectiveness of the mindfulness intervention, a mixed-methods, wait-list controlled protocol has been designed. Multiple groups will be facilitated to achieve a sample size of 50 dyads. Outcome measures will be taken across four time points: at 10 weeks and immediately prior to commencing the group, immediately after the intervention group, and at 1-month follow-up. Measures of depression and anxiety, perceived stress, emotional regulation, and positive psychological adjustment (benefit finding, post-traumatic growth) are included, as well as assessments of mindfulness levels and practice.

Results: To date, six dyads have commenced participation in the first mindfulness group intervention (response rate: 21%). The age range of participants is

58 -70 years (average 68.3), with 5 male and 1 female PwMND, and their MND-Fam members. Further intervention groups are planned for later this year and next year.

Discussion and conclusions: Factors contributing to the feasibility and efficacy of the mindfulness intervention groups developed to address the specific needs of pwMND and fmMND will be identified and discussed. Data analysis of the impact of the first two intervention groups will be available for conference presentation in December 2019.

Acknowledgements: We would like to thank the community of contributors and the fundraising team at Calvary Health Care Bethlehem for enabling the provision of this group research program.

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CP-18 Animal assisted activity with service dogs "One project" to heal the patients with ALS who have been hospitalized long term

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Keywords: palliative care, stress

Background: Our hospital is specialized for neurological intractable disorders. Most of patients stay in the hospital until they die. The trigger was an encounter with a service dog. We had a patient come to our outpatient clinic who was a service dog user. A nurse told me that there is a patient

with ALS living on mechanical ventilator who loves dogs very much but he did not have a chance to meet dogs. So we asked the service dog user to let her service dog "Chloe" meet him. She was glad to do so. When the ALS patient met Chloe he cried a lot and said "This is the happiest moment since I was admitted." We were deeply impressed and decided to start the animal assisted activity with dogs. The service dog user introduced us to the Japan Service Dog association. They agreed to cooperate, and two dogs and handlers started to come to our hospital every two months. We named this project as "One project".

Objectives: To heal patients with ALS in our hospital by animal assisted activity with service dogs

Methods: We have more than twenty ALS patients. Firstly, we asked them if they want to join the activity. Most of them were glad to join. We started AAA at the dayroom with about 10 patients together. Meanwhile we made a protocol for a private session. The dogs go to the bedside and climb on to the bed so patients can touch the dogs. We took patient's hand to touch dogs.

Results: All of them were so glad. They cried and laughed a lot. We asked how they felt after the session. Most of them answered that they felt so happy and could not wait for the next session. And one patient who had kept saying "I want to die" stopped saying so because he wanted to see the dogs again. Hospital staff were also happy watching the patients and dogs interacting and being happy.

Discussion and conclusions: We did not expect that a dog can give such great healing for ALS patients. And a dog gives healing to hospital staff also. A dog has ability to heal ALS patient's pain in the way we human cannot do so. We will keep trying to make patients' lives happier.

CP-19 Mental health support plans for people affected by MND

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Keywords: caregiver, coping, mental

Background: The author would like to present the final stages of a service development project intended to provide a mental health support plan for carers of people affected by MND. The initial findings of this project were presented at the ENCALS meeting in Tours, France, earlier this year.

Approximately 10% of people with MND may suffer from a mental health issue such as apathy (1), depression and anxiety during the course of their disease. However, over 30% of carers experience significant mental health issues when caring for someone with MND (2). This finding in particular has a detrimental effect on the wellbeing (both mental and physical) of the carer. The level of care they can provide diminishes, affecting the wider family group as well as attitudes towards health professionals. In order to alleviate this the author has developed a mental health support plan to assist carers of pwMND.

Mental health plans are implemented broadly in mental health care in the United Kingdom. A full literature search of existing mental health plans was performed. Although Borderline Personality Disorder is a very different condition to MND its' support plan is based on a series of symptoms or feelings the person may be experiencing. Therefore the framework of this established plan has been used to underpin the foundation of the MND Carer Mental Health support plan and in particular the psychological support that carers of pwMND need.

A short questionnaire and support plan is formulated during carer interview and produces a dynamic document which can be revised as situations change. It is anticipated that successful implementation of this support plan will:

- reduce worry
- reduce stress and distress for carers during the duration of the disease
- reduce the economic impact attached to carer burden as evidenced by Sue Ryder (3).

At the time of writing (June 2019) significant participation has been enjoyed with 65% of primary carers in the Highland region of Scotland opting to participate. Ongoing feedback is being collected as to the benefits of the support plan, why some people do not wish to participate, the incidence and reasons for drop outs and whether revisions to the support plan are necessary. The conclusion of these findings will be presented.

Acknowledgements: Funding for this project has been awarded by the Gordon Aikman Scholarship Scheme. With assistance from Robert Gordon University, Aberdeen, Scotland and Edinburgh University, Edinburgh, Scotland.

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CP-20 The needs and psychological distress of family caregivers after the death of the ALS patient

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Keywords: caregiver, depression, support needs

Background: ALS affects not just the patient, but also the patient's family who has to face the future loss of their loved one to this progressive and disabling disease. Furthermore, the patient often becomes highly dependent on the help and care delivered by the nearest relatives. That family caregivers may experience psychological distress, reduced quality of life and a high degree of burden when caring for a person with ALS is well-documented (1). However, the needs and psychological consequences of ALS for family caregivers surviving the death of the ALS patient are less clear.

Objectives: To review the literature for studies addressing the ongoing needs and psychological consequences experienced by family caregivers after the death of the ALS patient.

Methods: A systematic review of indexed articles to the PubMed and Scopus databases on the above subject published over the past 20 years from January 1999 until January 2019 will be performed. Reference lists of key articles will also be searched in order to identify relevant studies.

Results: Preliminary findings will be presented at the symposium.

Discussion and conclusions: The review may provide information on the long-lasting impact of ALS on family caregivers and whether long-term support from ALS clinics, health systems and ALS organizations is needed.

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CP-21 Support for patients with intractable neurological diseases to select treatment options

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Keywords: decision making, QoL

Background: In intractable neurological diseases, severe physical dysfunction tends to occur with the progression of the pathological condition, leading to difficulty in maintaining an independent daily life and social activities. Although the course varies among the diseases, patients are commonly forced to select treatment options (such as gastrostomy, artificial ventilation device use, and rehabilitation), which is a necessary process for them to maintain their lives and social activities, in order to fulfil themselves while coping with their diseases. This process of selecting treatment options mainly takes place at centres for the treatment of intractable diseases, and there have been large numbers of studies on support for patients with intractable neurological diseases to make their own decisions/declare their intentions and reports on home care support for them. However, the selection of medical/care procedures at these centres during the period from diagnosis to the end of life and the details of integrated and continuous

care based on such selection have rarely been examined.

Objectives: This study reviewed narratives regarding support for patients with intractable neurological diseases to select treatment options, with the aim of clarifying the expectations of this process among such patients (limited to those with 10 major diseases, for whom higher numbers of specific medical expense subsidy recipient certificates are issued), as well as the contents of related care.

Methods: The study design was a narrative review. Research papers on nursing were searched for, with the following keywords: ACP, decision-making/declaration of intention and selection of treatment options.

Results: Among the 28 Japanese papers identified, those on ALS accounted for the majority, discussing the challenges of selection and care related to the use of artificial ventilation devices and their discontinuation, gastrostomy, and home care. Among the 15 English papers identified, not only MND/ALS, but also MS was frequently observed, and these papers addressed challenges related to swallowing function and reproductive issues.

Acknowledgements: This work was supported by JSPS KAKENHI Grant Number JP 18K10364.

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Nagase M, Aoki K et al. 2014. 1-7

CP-22 Assessing preference heterogeneity with respect to MND treatment: A discrete choice experiment

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Keywords: SMA, decision making, healthcare

Background: The treatment of motor neurone diseases (MND), particularly spinal muscular atrophy (SMA), is being transformed by the development and availability of novel therapies. Understanding the range of factors that influence how patients make decisions is critical to ensuring medical care aligns with patients' preferences and values. This has been scarcely covered in the SMA literature and is important in promoting patient- and family-centred care and informing future policies and economic evaluations of SMA treatments.

Objectives: To quantify Australian patient, family, healthcare professional and community values for SMA treatments, and to understand if these values reflect societal preferences for the allocation of healthcare resources.

Methods: A binary discrete choice experiment (DCE) describes a hypothetical scenario and a possible treatment option. Given the described scenario, respondents indicate whether or not they would accept the treatment option offered (or recommend the treatment option, in the case of health professionals).

Attributes and levels used to describe the treatment options were developed using evidence derived from a series of focus groups with people with SMA, parents of children with SMA, and healthcare providers. Attributes covered five key aspects of SMA treatment: 1) potential benefits, 2) side effects, 3) costs, 4) novelty (ie whether the treatment is new or well-established), and 5) access to support. The overall binary DCE design comprised 32 treatment options, with each respondent randomly allocated 8 of these to limit participant burden.

Questionnaire validation among an Australian sample of the general public (n = 100), and a sample of patients, parents/carers and clinicians (n=50) is underway. Following completion of the pilot, a larger study including a random sample of the Australian public (n=1000), SMA patients (n=200), carers (n=200), and clinicians (n=50) will be conducted.

Recruitment of patient participants is through patient advocacy group advertising and clinicians from purposive sampling by an email invitation sent by the Australia and New Zealand Child Neurology Society. Survey Engine is hosting the survey and is facilitating recruitment of the representative Australian Population.

Results: Design and validation of the questionnaire will be presented.

Discussion and conclusions: In the face of a changing treatment landscape for SMA, it is essential to develop and implement research and clinical infrastructure that is sufficiently flexible to respond to these developments to maximise the potential benefits. This DCE investigates patient, family, health professional and community values and preferences in relation to treatment decision-making in SMA. With the pressures on health care budgets ever increasing, the results of this study will provide a basis from which to evaluate the potential cost impact and desirability of novel treatment strategies in MND.

Acknowledgements: Support for this research was provided by the Motor Neurone Diseases Research Institute of Australia

CP-23 The development of a multidisciplinary specialist communication and assistive technology (CAT) clinic within the New South Wales (NSW) public health sector

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Keywords: AAC system, assistive technology, CAT Clinic

Background: There are currently 56 clients with MND residing within South West Sydney Local Health District (SWSLHD) (MND Association NSW, 2019). Approximately 80% of clients with MND will present with dysarthria (1). The severity of impairment depends on the type of MND however most people become unable to speak and subsequently require a speech generating device to support verbal communication (2).

A high percentage of clients residing within SWSLHD are from culturally and linguistically diverse backgrounds (CALD). Clients were receiving less than optimal care within the existing service delivery model. The CAT clinic is currently the only NSW Health funded service available for people with MND offering occupational therapy and speech pathology multidisciplinary service.

Objectives: Meet the communication and assistive technology needs of clients with MND living in SWSLHD in a timely manner; maintain communication throughout disease progression and overcome barriers to communication for clients from CALD and low socioeconomic backgrounds.

Methods: Evaluation of existing services and gap analysis was completed within Australia. Clinicians benchmarked with similar private clinics. Clinicians applied for funding grants and donations to support equipment required within the CAT Clinic. Following approval from the health services and utilising existing resources, the CAT Clinic was established in October 2018. It services neurological and neurodegenerative populations and

operates once a fortnight with a total of 4 appointments offered.

Results: Since the establishment of the CAT Clinic, we have provided specialist assessments to 12 MND clients and an additional 14 reviews within an 8 month period. The average wait time for an initial assessment was 5.8 weeks.

Use of aided and unaided technology ensured that all clients with MND maintain communication across disease progression. Access to equipment loan pools has bridged the gap whilst awaiting permanent devices. The clinic has modified clinical practice to ensure clients from CALD backgrounds can access communication and assistive technology (e.g. utilising message banking and CALD communication software).

Discussion and conclusions: A specialist CAT clinic enables appropriate prescription of devices which are compatible throughout disease progression. It minimises incorrect prescription of devices and reduces length of time for prescription and intervention. A broad range of equipment is available for clients to trial at CAT Clinic with no product bias or financial gains. Additional funding for the setup of clinics is rarely available therefore innovative models of care are required to utilize existing resources and maximise client outcomes.

Acknowledgements: NSW MND Association and SWSLHD.

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CP-24 Occupational Therapist and the benefits of the online learning environment for clinical intervention for people living with MND

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Keywords: occupational therapy, support

Background: In 2018, an Occupational Therapist from Melbourne and the Sunshine Coast established an online network/forum for Occupational Therapists working with people living with MND in Australia. The online forum has gained over 250 members since its establishment and encourages clinicians to foster peer learning through resource and information sharing. Australia has rolled out of the National Insurance Disability Scheme over the past five years. The establishment of the online network enabled Occupational Therapists to share information and resources and share lived clinical experiences relating to service delivery for the unique service group that is people living with MND.

Objectives: To assess the relevance of an online learning environment/community forum for Occupational Therapist's working with people living with MND in Australia.

Methods: Online survey of 272 members, all Occupational Therapists registered to practice and who are currently delivering clinical intervention to people living with MND in Australia.

CP-25 How open ended questions posed by clients have informed, impacted and evolved an Occupational Therapy service from inception to now - 5 years on.

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Keywords: occupational therapy, clinical care

Background: The Metro South Motor Neurone Disease service was the development of unique service design in Queensland due to a lack of cohesive service provision. It consists of a domiciliary multi disciplinary team that provide ongoing proactive service in managing and supporting clients and their families through the changes as their disease progresses.

Occupation allows a person to adapt, cope, reflect, learn, live, do, appreciate, contribute, prioritise and fulfil their potential. It is through this lens that Occupational Therapists guide their interventions when working with people with Motor Neurone Disease. When at times, the best possible response an Occupational Therapist can provide is "I am not really sure the answer to that question, I will have to get back to".

Objectives:

- exposing the reader to reflect on the meanings they assign to 'doing=living' and how this can inform their practice
- exposing the reader to the concept of occupational deprivation and how they can use this to reflect and guide their practice
- exploring the value of being, in a person's life, as they adapt and adjust

- to the functional changes that Motor Neurone Disease will bring
- how exploring a client's roles can assist therapists to redefine their own, and therefore clients and family
- reflections on how clients may use other concerns or worries as a camouflage for deeper and more personal concerns
- providing examples of the use of the expert patient and shared decision making framework in clinical interventions with clients

Discussion and conclusions: It is through reviewing this poster, clinicians will have difficult questions posed to them, to reflect and evolve their individual practice.

CP-26 How an Occupational Therapy service has changed and evolved from direct client care provision to consultative service methods, to best meet the needs of people with Motor Neurone Disease post National Disability Insurance Scheme (NDIS)

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Keywords: occupational therapy, clinical care

Background: The Metro South Motor Neurone Disease service was the development of unique service design in Queensland due to a lack of cohesive service provision. It consists of a domiciliary multi disciplinary team that provide ongoing proactive service in managing and supporting clients and their families through the changes as their disease progresses.

When the introduction of the National Disability Insurance Scheme (NDIS)

occurred in Brisbane in July 2018, a change that has been described as the single biggest shake up to the health care sector in decades arrived. Even though Brisbane was one of the later geographical areas to be transitioned in Australia, there have been circumstances that no amount of planning or preparation could have readied the service for. When at times, the best possible response an Occupational Therapist can provide is “I am not really sure the answer to that question, I will have to get back to you”.

Objectives: Challenge the audience to review the: why; how; and when they deliver their therapy and interventions both currently and into the future

Methods:

- Capture the voice of clients and family who experienced grief and loss, due to a change in service providers and explore the factors that contributed to this
- Showcase real situations when consultative service methods have worked to enhance the bridge between the health and disability sectors of care
- Provide examples of the perception of other treating Occupational Therapists into the benefits and disadvantages of a consultative service method

Results: Readers will be challenged to reflect on their current service delivery method and have an insight into learning opportunities available with any large scale change.

Discussion and conclusions: Whole of system changes can and must to be translated to a local level, to tailor the solutions to meet the unique needs of each community.

**CP-27 OT for people with MND:
Adjusting and adapting to rapidly
changing function**

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Keywords: occupational therapy, assistive technology, multidisciplinary care

Background: Occupational Therapy (OT) has an important role in helping individuals and their families ‘adjust and adapt’ to the impact of a progressive neurological disease. MND is a rare and rapidly moving disease which requires a flexible and responsive approach to intervention. We often encounter OTs who report they lack confidence and/or skills to manage the needs of individuals with Motor Neuron Disease. This can be a confronting and demanding area of practice.

Objectives: We hope by sharing our experiences and knowledge in the area of neuropalliative rehabilitation we may assist our OT peers in understanding the specific care needs of this challenging population. The poster will focus on a best practice model of providing care and intervention for people with Motor Neurone Disease. Although this poster is about OT - the themes can be expanded to the MDT team.

Methods: Motor Neurone Disease (MND) is an umbrella term for different disease subtypes.

MND subtypes are characterised by often rapid and varying physical presentation and subsequent functional difficulties. Sound understanding of MND phenotypes assists in making appropriate decisions regarding choice and timing of OT interventions. We reviewed the literature and used personal and professional experience to compile information summary for the poster.

Results: MND is an incurable condition and the subsequent resulting disability has a massive impact on all aspects of a person’s being and ability to participate in previously held life roles. Rate of disease progression

can be rapid requiring a flexible and responsive approach. Working in this area of care provides many challenges including:

- Constant change in functional abilities.
- Accessing funding, carer demands and specialised equipment needs.
- Grief, loss and emotional adjustment to devastating diagnosis.
- The understanding of MND phenotypes to guide clinical reasoning.

Discussion and conclusions:

Motor Neurone Disease (MND) is an incurable but not untreatable progressive neurological condition.

Working with people who have been diagnosed with MND can be a challenging, demanding and confronting area of practice for Occupational Therapists:

- Clients with MND require a flexible, responsive and ongoing OT input
- The rapid progression of this disease results in significant functional decline
- There may be limited time to adjust to change before next change occurs
- Vast array of presenting deficits depending on phenotype and onset location
- Individual reactions to diagnosis may differ greatly - introduction of aids and equipment may require gradual introduction, gentle discussion and negotiation
- Large challenges for funding equipment and supports in a timely manner
- Huge psychological adjustment to neuro- palliative diagnosis for the individual and their significant others

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[pter/Recommendations#managing-symptoms](#)

CP-28 Reflections on the care of people with MND/ALS care over 35 years

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Keywords: care team, clinical care, developments

Background: Over the last 35 years the care provided for people with MND/ALS has improved and there are now interventions that may improve both the quality and length of life

Objectives: There are many issues which need to be discussed openly so that all involved in MND/ALS care – patients, families and professional teams, can together develop ways of coping.

Methods: The aspects of care are reviewed from the experience of the author and the literature.

Results: Areas to consider include:

Genetics - the possibility of identifying a gene mutation has increased and now 60% of people with a familial history may identify the particular gene involved. This now raises ethical issues. Diagnosis - the giving of the diagnosis is never easy but good information will help reduce the myths of the distressing nature of living with and dying from MND/ALS.

Nutrition - there is increasing evidence that nutrition has an important influence on morbidity and mortality, necessitating discussion of nutritional supplementation and the discussion of gastrostomy for patients with dysphagia. Respiratory support - the majority of people in the past died of respiratory failure, often related to

infection. The role of non-invasive ventilation, and on occasions invasive ventilation with a tracheostomy, has increased with many benefits of symptom management, but also increasing ethical issues of the consideration of withdrawal at the end of life. Multidisciplinary team care - there is increasing evidence that MDT approach is very helpful in supporting patients and their families, with improvement in both quality and length of life.

Advance care planning - there is often reluctance to discuss advance care planning so that the person's wishes are known if they should lose the capacity to make decisions for themselves. As communication and cognition may be affected these discussions are very important. End of life care - the care at the end of life may be complex, as there may be difficulties, and reluctance, to recognise that death is approaching. The management of symptoms and the support of all involve is essential.

Assisted dying - there is increasing discussion about the role of assisted dying – euthanasia and physician assisted suicide – for people with MND/ALS. Many ethical and decision-making issues arise. Palliative care - there has been a long debate of the role of palliative care in MND/ALS. There is now increasing agreement that there is a role throughout the disease progression, according to specific need, rather than just at the end of life. There is also increasing evidence of its effectiveness.

Discussion and conclusions: There have been many changes, but the basics of care – listening to the patient and family and helping them to make decisions based on good information with time to deliberate - remains. There may be still a long way to go!

CP-29 Four quadrants of care

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Keywords: multidisciplinary care

Background: The Metro South Chronic Disease MND service is a community based multidisciplinary team that supports clients and their families throughout the whole duration of their disease. This presentation highlights four quadrants of care and the benefits and the challenges involved in being a responsive multidisciplinary team. From this, a clearer idea of what that looks like when providing high quality ongoing care for patients with MND and their families will be determined.

The interventions implemented to achieve the above are multi-factorial and will be explored on a deeper level throughout this presentation.

Rooney et al (2015) concluded that a centralised multidisciplinary team provides a survival advantage of 7 – 24 months for patients with MND which we aim to achieve.

The four areas of discussion to be explored are;

- the communication between team members, hospital staff / departments and the patients/families, and the development of the clinical feedback processes,
- the development of collaboration between external organisations and other hospitals and how this affects patient care
- the community team have taken on the role of triaging the hospital clinic which has significant benefits and challenges which will be thoroughly discussed, and how we have resolved some of these challenges
- how the team provides responsive high quality ongoing care for patients in order to achieve Rooney's goal

CP-30 Shhh...we don't talk about that !

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Keywords: symptom management, sexuality

Background: The Metro South MND service is a multidisciplinary team that provides an ongoing proactive service in managing and supporting clients and their families through the changes as their condition deteriorates. All our care and visits are provided in their home environment which is much easier for the client and being in their environment enables them to feel safe and more open in their thoughts and feelings.

Guidelines encourage the promotion of maintaining sexuality and intimacy, however very little is actually written about how to manage this. Situations that arose that initiated my interest were;

'Yes I have MND but I don't have to worry about falling pregnant surely?'

'My hubby is struggling with changing pads, never mind sanitary products'

'My wife is 3 months pregnant!'

'The worst thing about MND is having an erection I can't do anything about'

The aim of this presentation is to raise the awareness of issues that can arise. How do we discuss contraception, menstruation, pregnancy and sexual needs? Many of these subjects are not always easy for clinicians to discuss, due to lack of experience, knowledge, embarrassment, and knowing in some areas there are no magic answers.

However, I want to discuss what are the implications of pregnancy, both for the client if they became pregnant, the client when their partner becomes pregnant, managing menstruation, and not having sexual needs met? I will explore this area and our experiences in order to raise awareness of the topics and increase knowledge with the aim of improving patient care and give clinicians additional skills and confidence in discussing these issues.

CP-31 Metro South chronic disease MND gastrostomy change service

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Keywords: clinical care, gastrostomy

Background: The Metro South MND service is a multidisciplinary team that provides an ongoing proactive service in managing and supporting clients and their families through the changes as their condition deteriorates. All our care and visits are provided in their home environment which is much easier for the client. However, clients that have gastrostomy tubes previously had to attend the Princess Alexandra Hospital to have their tube changed every 4-6 months.

Getting to the PA hospital is extremely difficult for many due to transport, time and fatigue, especially as their disease progresses and getting places becomes much harder. Once clients become wheelchair dependant and do not have their own adapted vehicle, they have to rely on community transport or ambulance transport which is not responsive in drop off and pick up times around their appointment times.

There can be a lot of waiting time in the radiology outpatient unit which can lead to an increase risk of pressure injuries and issues with care needs. MND clients can get very fatigued so all the travelling and waiting around can exacerbate the fatigue

Objectives: The aim was to create a pathway whereby clients could have their tubes changed at home, thus negating the need for travel and creating a person-centered service

Methods: I will describe our initiative and how we created the service

Results: The results to date have been extremely positive, both from clients and their families and were achieved using patient satisfaction questionnaires.

CP-32 A dying wish: Organ donation in MND - ethics law and practice in the Australian context

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Keywords: ethics, decision making, organ donation

Background: In best practice settings, persons with MND are encouraged and enabled to have careful and comprehensive discussions with their clinical teams and carers regarding their end of life wishes and preferences. In this context, the wish to be an organ donor is arguably an important issue to consider, though it is unclear how often this is discussed, and even where raised, how it is explored or considered. We describe the sentinel case study of a person with MND whose wish to be an organ donor was considered, explored, and enabled - as donation after circulatory death in the context of first person consent and timed withdrawal on non-invasive ventilatory support. Consequent to this case, we are developing a process for persons with MND in our jurisdiction to be able to explore and consider the option of organ donation in their unique circumstances. This paper details the ethical, legal, organisational and practical considerations as they relate to our jurisdiction, and proposes the key components to consider in enabling this option to be available to persons with MND who wish to consider it.

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