Use of pharyngeal high resolution manometry to evaluate dysphagia in adults with Motor Neurone Disease: A scoping review

Declaration of interest: The authors have no relevant financial or non-financial interests to disclose.

Funding: No funding was received for conducting this study.

Conflicts of Interest: The authors have no potential conflict of interest to report.

Financial interests: The authors declare they have no financial interests

Acknowledgements: Thanks to Isolde Harper, subject librarian in Trinity College Dublin who provided support with the search strategy.
Abstract

Objective: There has been a recent shift towards proactive dysphagia intervention in motor neurone disease (MND) to maintain physiological reserve. Pharyngeal high-resolution manometry (PHRM) can quantify swallowing pathophysiology to inform and evaluate proactive dysphagia intervention. This study aims to explore the current use of PHRM as a dysphagia evaluation in adults with MND.

Methods: A scoping review based on the Joanna Briggs Framework was completed. Four electronic databases (PubMed, EMBASE, CINAHL and Web of Science core) were searched (inception to March 2021) by two independent researchers. Data was analysed according to (i) PHRM protocol and analysis methods and the feasibility of same, (ii) swallow biomechanics data and (iii) dysphagia intervention effects as measured by PHRM.

Results: Six studies with 78 people with MND (PwMND) were included. There was considerable variation in PHRM protocol and analysis methods. Five studies reported a 100% completion rate and three studies reported no adverse events. Swallow biomechanics data was reported across all studies. The effects of sensory stimulation, increased bolus consistency, effortful swallow and cricopharyngeal myotomy were evaluated using PHRM with 20 PwMND across four studies with varying effects.

Conclusion: Literature on the use of PHRM in PwMND is limited. Variability in PHRM methods restricts comparison of metrics. PHRM appears to be a feasible tool for PwMND. PHRM can provide novel swallow physiology data in PwMND and quantify discrete effects of compensatory and surgical dysphagia interventions not detectable by videofluoroscopy or FEES. Further research on the effects of proactive dysphagia intervention as measured by PHRM is required.

Key words: deglutition; deglutition disorders; pharyngeal high resolution manometry, motor neurone disease; amyotrophic lateral sclerosis
Introduction

Motor neurone disease (MND) is a life-limiting neurodegenerative condition characterized by the progressive decline of the motor neurones [1]. MND progresses rapidly, with average survival estimated at 2 to 4 years post-diagnosis [2]. The International Statistical Classification of Diseases and Related Health Problems (ICD-10) acknowledges four subtypes of MND [3]. Amyotrophic Lateral Sclerosis (ALS), is the most prevalent of the subtypes. The remaining subtypes include Progressive Bulbar Palsy, Progressive Muscular Atrophy and Primary Lateral Sclerosis [3]. At this point in time, there is no reversible treatment for what is typically a catastrophic collapse of a previously apparently normal functioning motor system. Symptomatic management is the main course of treatment [4]; thus, identification and exploration of mechanisms of impairment by researchers and clinicians are of significant importance.

One of the most frequent and devastating symptoms of MND is dysphagia, a group of symptoms characterised as difficulty forming the bolus and progressing it safely and efficiently from the mouth to the stomach [5]. Evidence suggests that almost all people with MND (PwMND), regardless of subtype, will eventually experience some degree of dysphagia [6]. Dysphagia in MND may occur during any stage of the swallow due to the weakening of the bulbar, respiratory and limb musculature [7, 8]. As MND progresses, individuals will experience a worsening of dysphagia symptoms, leading to complications such as dehydration, weight loss, malnutrition and aspiration pneumonia [1, 8]. Indeed, aspiration pneumonia is the leading cause of death in this clinical population [9].

Traditionally, a compensatory approach has been taken to dysphagia management in the MND population. As part of this disease-centric reactive approach, the focus has been on palliative interventions [7]. In an effort to optimise physiological reserve for swallowing early in the disease process, there has been a recent shift towards pro-active dysphagia management [10]. This approach involves proactively targeting underlying physiologic function before the development of dysphagia to optimise physiological reserve. To accommodate for this shift in dysphagia management, an instrumental dysphagia evaluation which can capture discrete alterations to swallow physiology from early stages of the disease is needed to identify therapeutic targets in dysphagia treatment.

Pharyngeal high-resolution manometry (PHRM) is an emerging technology gaining increasing interest as a method for assessing pharyngeal swallow function [11]. In contrast to videofluoroscopy (VFS) and fiberoptic
endoscopic evaluation of swallowing (FEES), which focus largely on swallow safety and efficiency, PHRM objectively identifies abnormalities in pharyngeal function through the quantification of pressure changes across the pharynx. To date, PHRM provides novel data on the velopharynx, mesopharynx, hypopharynx and the UES [12], all of which are affected in the MND population [1]. PHRM can clarify the biomechanical foundations of dysphagia that cannot be understood from visualisation alone, which would contribute to an enhanced, more targeted intervention plan for the PwMND.

While PHRM would ensure the identification of subtle physiological changes of the swallow in PwMND, which, with the progressive nature of MND, could prove integral in preventing devastating dysphagia complications, there is a significant gap across the literature summarising the adoption of PHRM into dysphagia evaluation in PwMND. Such research is vital. PHRM is an invasive procedure and prevalent features of MND such as weak cough and hyperactive gag reflex could potentially impact patient acceptability and thus the overall feasibility of this assessment for PwMND [6,7].

The primary aim of this study is to explore and summarise the use of PHRM to evaluate dysphagia in PwMND. In doing so, the following research questions will be addressed:

(1) What PHRM protocol and analysis methods are currently being used with PwMND and are they feasible for this clinical population?

(2) What are the swallow metrics obtained from PHRM in PwMND and how do these compare to metrics from healthy adults?

(3) What are the effects of swallowing interventions in PwMND as measured by PHRM?

Methods

Methodological approach

A scoping review was completed based on the methodological framework by the Joanna Briggs Institute (JBI) [13]. The JBI framework provides more explicit detail of the methodological steps than prior frameworks. This enhancement of detail increases the rigor and clarity of the review process and was thus selected for this study. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) [14] was also used to highlight potential methodological issues and enhance the reporting quality of this paper (see appendices).
**Inclusion Criteria**

- Studies involving adults (>18 yrs) that presented with any subtype of MND, under the ICD-10 code G12.2 [3], that underwent PHRM as an oropharyngeal swallow assessment or as a measure of intervention effects from which pressure metric data could be extracted were included in this study.
- No constraints were applied regarding the geographical location of the study or the year of publication.
- Abstracts of studies yet to be published were included provided sufficient data could be drawn.
- Studies reporting data on a heterogeneous population that included some participants with MND were included.
- Studies documenting metric data were included regardless of what oropharyngeal metric data they provided, so long as they reported on at least one UES or pharyngeal metric.
- Papers that report the use of PHRM with or without impedance were included.
- Records investigating the effects of any intervention type; rehabilitation, surgical, compensatory and/or environmental were included, provided adequate data was provided.

**Exclusion criteria**

- Studies using water perfused manometry, balloon-based manometry or 3D PHRM systems were excluded. Based on the PHRM international working group’s recommendations, studies that use solid-state manometry with less than ten pressure sensors more than 1cm apart were excluded [15].
- Review papers or papers presenting previously published data were excluded (e.g., [16]).
- Studies that did not provide extractable quantitative metric data on the PwMND and whose authors could not provide such data or did not respond were excluded.
- Studies published in any language other than English were excluded.

**Search Strategy**

A comprehensive search string was developed by the researcher and peer-reviewed by a qualified university research librarian using the PRESS-EBC Checklist [17]. All included search strings are listed in the appendices section. The search strategy applied in PubMed is reported as an example (performed on 10/03/2021)

deglutition*[Title/Abstract] (T/A) OR swallow* (T/A) OR oropharyngeal (T/A)OR pharyn*(T/A) OR dysphagi*(T/A) OR feed*[T/A) OR fed (T/A) OR eat (T/A) OR eating (T/A) OR eats (T/A) OR ate (T/A) OR
drink*(T/A) OR drank(T/A) OR deglutition[MeSH Terms] OR deglutition disorder[MeSH Terms]) AND (mixed etiolog*(T/A) OR mixed aetiol*(T/A) OR motor neurone disease*(T/A) OR motor neuron disease*(T/A) OR MND (T/A) OR ALS (T/A) OR motor system disease*(T/A) OR anterior horn cell disease*(T/A) OR lateral sclerosis (T/A) OR lateral scleroses (T/A) OR progressive bulbar palsy (T/A) OR bulbar paralysis(T/A) OR progressive muscular atroph*(T/A) OR charcot disease*(T/A) OR Lou Gehrig (T/A) OR motor neuron disease[MeSH Terms]) AND (manometry (T/A) OR high resolution(T/A) OR pharyngeal pressure*(T/A) OR manometry[MeSH Terms])

**Procedure**

**Information sources:**

Four electronic databases were searched from the inception of the database to the 10TH of March 2021, including PubMed, EMBASE, CINAHL, and Web of Science Core. No limits, i.e., language or date were put on the search. The Dysphagia Journal and the Amyotrophic Lateral Sclerosis Journal, as well as the 2020 published conference abstracts of the Dysphagia Research Society (DRS) (available via DRS website) and the European Society of Swallowing Disorders (ESSD) (available via the ESSD website) were reviewed. The bibliography of all the identified publications were screened by the titles and citations were tracked via the Google Scholar website. All searches were conducted by the primary researcher (ED).

**Screening the evidence:**

All retrieved citations were imported into EndNoteX9 software [18] for data management and storage. Citations were exported to Covidence [19] for removal of duplicates and screening. Title and abstracts and full texts were screened by two independent researchers (ED)(JR). A full 100% agreement level was achieved. The final data extraction was performed by an independent researcher (ED).

**Data synthesis:**

Due to the heterogeneity in PHRM protocol and equipment and the ability for technique or catheter configuration to impact results, this review concentrated on regional changes in relation to swallowing outcomes. This knowledge should be considered when interpreting the metric data and as such, rather than conducting a statistical synthesis, a narrative analysis was performed.
PHRM protocol and analysis methods, metric results of PwMND and intervention effects were tabulated, interpreted and given meaning through discussion and description in the narrative texts. Data regarding the feasibility of the assessment was also analysed and descriptively discussed.

The metric results of PwMND were analysed and compared against the normative data outlined in that same study; this was to establish consistency across PHRM protocol and analysis methods and thus ensure true comparability of results. The comparisons were translated into a bar chart graphic to enable visualisation and further exploration of the changes in the swallow in PwMND.

Results

Selection of sources of evidence

A total of 143 studies were identified from the search across the aforementioned databases, journals, conference abstracts and reference lists. After deduplication, 115 studies remained. A total of 72 studies were excluded after title abstract screening, leaving 43 studies for full-text review. Eventually, 6 studies, one of which was an abstract of a study yet to be published, remained and were included in this review. Figure 1 illustrates the PRISMA flow diagram of study selection.

Figure 1 here

Of the 6 studies included, 1 was a single case study [20], 2 were case-control study designs [21, 22] and 3 were quasi-experimental designs (pre-test-post-test designs) [23-25]

Participant demographics

There was considerable variation concerning sample size across studies; on average, studies included 11 participants with MND. Male patients constituted 54% of patients across studies; this accurately represents the Male: Female predominance in MND [26]. The average age of patients across studies was 68±10 years; this too is representative of the MND population as the peak incidence of MND falls between 60-75 years [27]. Documentation on dysphagia severity varied across studies. 50% of studies outlined the participants functional oral intake scale (FOIS) severity, FOIS 1 being nil by mouth and FOIS 7 being total oral diet. Further information regarding patient demographics is outlined in Table 1.

Table 1 here
**PHRM protocol and analysis methods & the feasibility of such methods for PwMND**

All 6 studies are included in the PHRM equipment and data acquisition section. 5 studies are included in the feasibility section.

**PHRM Equipment**

The majority of studies did not provide full documentation of the PHRM equipment used. Variability in the type of PHRM equipment used was noted across studies that did report such information. Of the studies that documented PHRM system, the Mano scan was most reported (50%) followed by the MMS solar (33.3%) and Insight (16.6%) systems. Further information on PHRM equipment reported across studies is outlined in Table 2.

**Data Acquisition**

Variability in the protocol of data acquisition and documentation of this protocol across studies was also noted. 42.9% of studies reported the use of Topical Nasal Anaesthetic (TNA). The type of TNA was documented in 66.6% of these studies. Type ranged from lidocaine spray in one study [21] to co-phenylalanine forte spray and lignocaine gel in another [22]. 57% of studies used a 5ml bolus volume, 28% used 10ml and 14% used dry swallows. The variability in the protocol of data acquisition is further outlined in Table 2.

**Table 2 here**

**Data Analysis**

The Analysis software used across studies is outlined in Table 2. One study [20] utilised the ManoView software. This software requires correction of a system based measurement fault [28]. The study did not state whether the correction was made.

*Analysis of the pharynx.* Each of the 6 studies documented at least one pharyngeal measurement. Figure 2 illustrates the different pharyngeal metric sites and measurement parameters documented across the studies and the percentage of studies that reported each. The highest number of studies to report on the same exact
parameter i.e., velopharyngeal contractile integral, was 33.3% (2 studies).

**Figure 2 here**

*Analysis of the UES.* Each study reported on the UES. The UES measurement parameters documented across studies and the percentage of studies that reported each is presented in Figure 3. The number of studies reporting on the same measurement parameter of the UES (83.3%) was greater than that of the pharyngeal measures, however, differing definitions of this UES parameter (UES Integrated relaxation pressure) was noted across studies.

**Figure 3 here**

*Feasibility*

One study [25] an abstract only, did not report PHRM outcomes. All of the remaining 5 studies documented a 100% completion rate of PHRM in participants with MND. Adverse events were reported in 60% of studies; 100% of these studies reported that no side effects or adverse events occurred as a result of PHRM. One study documented patient tolerability reporting that the patients tolerated the assessment well. None of the included studies documented participant-reported outcomes of the assessment.

*Swallow Biomechanics*

*Biomechanics of the swallow in PwMND:*

6 studies are included in this section. A comprehensive overview of the PHRM metric results of PwMND reported across these studies is provided in Table 3.

**Table 3 here**

*Biomechanics of the swallow in PwMND compared to normative data:*

As data on a healthy control group was not included in 2 of the studies [23, 24], 4 studies are included in this section. Takasaki and colleagues [20] included retrospective normative data established in their previous study; the remaining papers established the normative data in the study included. All studies including normative PHRM metric data used the same PHRM protocol and analysis methods with the healthy participants and the PwMND.
Figure 4 and Figure 5 outline the comparison between PHRM metric results in PwMND and healthy participants. Further detail on the metric results of the healthy participants is presented in Table 3.

**Figure 4 here**

**Intervention effects**

The effects of interventions in PwMND as measured by PHRM are discussed under the following four intervention categories; (i) Change to bolus characteristics, (ii) swallowing manoeuvres, (iii) surgical interventions and (iv) behavioural interventions. Four studies documented intervention effects and are thus included in this section. Table 4 outlines the effects of the various interventions.

**Table 4 here**

*Change to bolus characteristics*

**Sensory Stimulation.** One out of the two PwMND in Regan's [23] study could not tolerate sensory stimulation. Data from the remaining participant is reported in Table 4. Cold, sour and carbonated boluses caused a considerable increase on the velopharyngeal mesopharyngeal and global pharyngeal contractile vigour. Sensory stimulation did not alter the hypopharyngeal contractile integral as significantly, except the carbonated bolus, which increased this measure.

**Altering bolus consistency.** Normal saline liquid and viscous boluses were trialled with PwMND in Cock and Colleagues' [22] study. The addition of viscosity resulted in a reduction in pharyngeal peak pressure in PwMND. Effects of the viscous bolus on the swallow of PwMND can be found in Table 4.

**Manoeuvres**

**Effortful swallow.** Both PwMND included in Heslin's [24] study tolerated and completed the effortful swallow manoeuvre. UES relaxation duration was increased in both participants when the manoeuvre was applied. Further effects of such are outlined in Table 4.

**Surgical**

**Cricopharyngeal myotomy.** Takasaki et al. [20] evaluated the swallowing pressure in a patient with MND one month before and three months after bilateral cricopharyngeal myotomy. As outlined in table four, the patient's
velopharyngeal pressures did not change after surgery. The values of the UES, on the other hand, decreased significantly.

**Discussion**

This study sought to explore the use of PHRM to evaluate dysphagia in PwMND. The inclusion of six publications, half of which contained a sample size of two or less participants, suggests that the current use of PHRM to evaluate dysphagia in PwMND is quite limited. This is despite the fact there has been a recent shift towards proactive dysphagia management in PwMND to optimise physiological reserve. As PHRM is being adopted into clinical practice internationally [29], the use of PHRM to evaluate dysphagia in this clinical population is likely to increase in the future.

Several important findings based on this limited data are highlighted in this review. This scoping review has demonstrated considerable variability in PHRM protocol and analysis methods in PwMND. There was variability in HRM systems used, HRM catheter dimensions, bolus volumes and consistencies administered and PHRM metrics obtained. Each of these variables can alter the pressure measurements obtained, limiting comparison of study findings [15]. Winiker et al. [28] reported considerable variability in PHRM protocol and gaps in documentation of such protocol across the literature. This review reveals that studies using PHRM in PwMND are no exception to these gaps or discrepancies.

PHRM is an emerging technology and standardised guidelines for protocol and analysis methods have yet to be fully established. The PHRM international working group published the first set of protocol and metric recommendations which may streamline PHRM protocols in future dysphagia research [15]. A 5 minute accommodation period, bolus delivery via syringe and the use of a solid state HRM system with at least 10 pressure sensors 1cm apart is advised. The magnitude of variability in the PHRM protocol and analysis methods and gaps in the documentation of such across the included studies is likely due to the fact that four out of six of the studies were published before these recommendations. One of the remaining three studies is an abstract only [25], thus justifying its lack of documentation. It is encouraging to note that full compliance to the recommendations was noted in the outstanding studies [23,24], suggesting that the most recent publications are adhering to these preliminary guidelines. Continued compliance to the working groups' recommendations in future publications will increase comparability of results across papers and will, in turn, enhance and further improve the understanding of the nature and course of dysphagia in PwMND.
From a PHRM feasibility perspective, PwMND across all FOIS levels, in all studies that documented outcomes completed the PHRM assessment. Furthermore, the studies that reported adverse events reported that no side effects or adverse events occurred. This finding suggests that despite bulbar dysfunction in MND, PHRM is a feasible tool for this clinical population. This finding has somewhat been reflected in the previous literature. Transnasal endoscopic procedures pose similar risks to the transnasal passage of the PHRM catheter [30]. Studies documenting such procedures in PwMND have reported a high completion rate and low incidence of adverse events [31, 32]. The advancement of the PHRM catheter through the UES, which is not seen in FEES, introduces additional considerations [30]. While this is the first study to outline the feasibility of PHRM in PwMND, previous studies have documented a high completion rate of PHRM in people with dysphagia, concluding that it is a safe and practical assessment [30]. It is of interest, however, that only one study documented patient tolerability and none of the included studies documented patient-reported outcomes of the assessment. This is a striking finding and researchers should be aware that data regarding patient tolerability is integral for an assessment that is translating into clinical practice [28]. Capturing the patients' experience holds increased importance for this clinical population as features of MND such as hyperactive gag reflex and weak cough may impact patient acceptability significantly [6,7]. Thus, while the limited data obtained suggests that PHRM is a feasible tool, gaps in documentation of patients' experience obscures the certainty of this finding.

PHRM was used across studies to provide quantitative novel data on the velopharynx, mesopharynx, hypopharynx and the UES in PwMND. The aforementioned variability in protocol and analysis methods restricts the comparability of the metric results across the studies. Nevertheless, preliminary data published to date suggests that alterations in swallow pressure are present, they can be identified in the velopharynx, mesopharynx and hypopharynx during swallowing. PHRM therefore has the potential to provide clinically useful quantitative data on swallow pathophysiology, that cannot be captured through VFS or FEES. This data has the potential to inform proactive dysphagia intervention in this population to maximise physiological reserve.

When compared against normative data, the most dominant changes in swallowing physiology in PwMND highlighted through PHRM included (i) reduced pressure and contractility in the mesopharyngeal, hypopharyngeal and global pharyngeal region and (ii) evidence of UES restriction. These findings somewhat align with the previous literature as 'changes in muscle tone' and 'reduced constriction' have been previously reported [1,7,8]. However, this comparison further highlights that PHRM provides enhanced insight into the
swallowing physiology in PwMND, as regional detail on pressure changes and exact, reliable findings of the UES have not been summarised in the literature before. While these findings are based on limited data and further research is required to delineate the nature of these results, it can be concluded that PHRM offers an enhanced, comprehensive and specific insight into the changes of the swallow in PwMND.

This review highlights the potential role of PHRM to determine the discrete benefits of dysphagia interventions on swallowing in PwMND. To date, PHRM has been used in four studies to delineate specific effects of surgical and compensatory dysphagia interventions, including cricopharyngeal myotomy, sensory stimulation, increased bolus consistency and effortful swallow. The impact of cricopharyngeal myotomy on PwMND has been previously documented in a dated VFS study; reported findings were vague as the procedure was documented to 'improve swallow function' [42]. This review highlights that PHRM provides a much more specific and objective account of the effects of the intervention. The quantitative effects of the cricopharyngeal myotomy on the UES and velopharyngeal regions in the participant with MND were provided in the included PHRM study, rather than a descriptive subjective claim of improvement. The impact of thickened liquids has been reported to reduce pharyngeal constriction in PwMND in a VFS study [34]. These findings somewhat align with the results of the included PHRM study as reduced pharyngeal pressures were reported in response to increased bolus consistency in PwMND [22]. The PHRM study, unlike the VFS study, provided an insight into the quantitative degree of reduction, enabling a more comprehensive and definite insight into the effects of the intervention.

Further research into the effects of proactive dysphagia interventions on PwMND as measured by PHRM would increase clinician and researchers understanding of the nature and impact of dysphagia interventions and would ensure that only the most beneficial interventions are applied.

The findings of this review carry clinical significance as they inform clinicians of the value and viability of completing the PHRM assessment with PwMND. This review suggests that PHRM is a feasible tool for PwMND that can be utilised by clinicians to obtain a specific insight into the biomechanics of the swallow as well as an overview of the discrete and subtle effects of dysphagia interventions.

This scoping review of the adoption of PHRM into dysphagia evaluation in PwMND is the first of its kind and serves as a basis for guiding future research in this field. In order to enhance the understanding of the use of PHRM in PwMND, future research should focus on the feasibility of PHRM in this clinical population, highlighting patient acceptability and patient reported outcomes of the assessment. Researchers should adhere to the PHRM international working groups recommendations and follow the protocol and select the metrics that
are advised. Given the small sample sizes across all included studies, it is recommended that researchers come together and collaborate to conduct large scaled multi-site research. This would increase the sample size, the quality of the research and in turn our understanding of the use of PHRM to evaluate dysphagia in PwMND.

**Conclusion**

Few studies have reported the use of PHRM in PwMND, thus, it can ultimately be concluded that the current understanding of the adoption of PHRM into dysphagia evaluation in PwMND is limited. While variability in PHRM protocol and analysis methods in PwMND restricts the comparability of the metric results, PHRM appears to be a feasible tool for this clinical population. PHRM can provide novel data on the swallow biomechanics in PwMND, offering an enhancing and detailed insight into the subtle and specific physiological changes in the swallow that occur in PwMND. Additionally, given the recent move from compensatory dysphagia management in this population, PHRM may identify therapeutics targets and quantify benefits to proactive rehabilitation. Further research is required to advance the understanding of the adoption of PHRM into dysphagia evaluation in PwMND.
References:

1. Waito AA, Valenzano TJ, Peladeau-Pigeon M, Steele CM (2017) Trends in research literature describing dysphagia in motor neuron diseases (MND): a scoping review. Dysphagia 32(6):734-747. https://doi.org/10.1007/s00455-017-9819-x.

2. Lisiecka D, Kelly H, Jackson J (2019) How do people with motor neurone disease experience dysphagia? A qualitative investigation of personal experiences. Disabil Rehabil 1-10. https://doi.org/10.1080/09638288.2019.1630487.

3. World Health Organisation (2015) International statistical classification of diseases and related health problems (10th Revision). WHO. http://apps.who.int/classifications/icd10/browse/2016/en. Accessed 2020 Oct 15.

4. Valadi N (2015) Evaluation and management of amyotrophic lateral sclerosis. Prim Care 42(2):177-187. https://doi.org/10.1016/j.pcr.2015.01.009.

5. Romero-Gangonells E, Virgili-Casas MN, Dominguez-Rubio R, Povedano M, Pérez- Saborit N, Calvo-Malvar N, Barceló MA (2020) Evaluation of dysphagia in motor neuron disease review of available diagnostic tools and new perspectives. Dysphagia 21(3): 135-143. https://doi.org/10.1007/s00455-020-10170-7.

6. Chen A, Garrett CG (2005) Otolaryngologic presentations of amyotrophic lateral sclerosis. Otolaryngol Head Neck Surg 132(3):500-504. https://doi.org/10.1016/j.otohns.2004.09.092

7. Kühnlein P, Gdynia HJ, Sperfeld AD, Lindner-Pflieghar B, Ludolph AC, Prosiegel M, Riecker A (2008) Diagnosis and treatment of bulbar symptoms in amyotrophic lateral sclerosis. Nat Clin Pract Neurol 4(7):366-374. https://doi.org/10.1038/ncpneuro0853.

8. Waito AA, Plowman EK, Barbon CEA, Peladeau-Pigeon M, Tabor-Gray L, Magennis K, Robison R, Steele C (2020) A cross-sectional, quantitative videofluoroscopic analysis of swallowing physiology and function in individuals with amyotrophic lateral sclerosis. J Speech Lang Hear Res 63(4):948-962. https://doi.org/10.1044/2020_jshr-19-00051.

9. Corcia P, Pradat PF, Salachas F, Bruneteau G, Forestier N, Seilhean D, Hauw JJ, Meininger V (2008) Causes of death in a post-mortem series of ALS patients. Amyotroph Lateral Scler 9(1):59-62. https://doi.org/10.1080/17482960701656940.

10. Rogus-Pulia NM, Plowman EK (2020) Shifting tides toward a proactive patient centered approach in dysphagia management of neurodegenerative disease. Am J Speech Lang Pathol 1094-1109. https://doi.org/10.1044/2020_AJSLP-19-00136.

11. Davidson K, O’Rourke AK (2019) The Utility of high-resolution pharyngeal manometry in dysphagia treatment. Perspectives of the ASHA Special Interest Groups 4(3):507-516. https://doi.org/10.1044/2019_PERS-SIG13-2018-0027.

12. Doelggen SH, Ong E, Scholten I, Cock C, Omari TI (2017) Biomechanical quantification of mendelsohn maneuver and effortful swallowing on pharyngoesophageal function. Otolaryngol Head Neck Surg 157(5):816-823. https://doi.org/10.1177/0194599817708173.

13. Peters MDJ, Godfrey C, McNerney P, Munn Z, Tricco AC, Khalil H (2020) Chapter 11: scoping reviews [Internet]. In: Aromataris E, Munn Z, (ed) JBI manual for evidence synthesis. https://doi.org/10.46658/JBIMES-20-12.

14. Tricco AC, Lillie E, Zarin W, O’Brien KK, Colquhoun H, Levac D, Moher D, Peters MD, Horsley T, Weeks L et al. (2018) PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med 169(7):467-473. https://doi.org/10.7326/m18-0850.

15. Omari TI, Ciucci M, Gozdzikowska K, Hernández E, Hutcheson K, Jones C, Maclean J, Nativ-Zeltzer N, Plowman E, Rogus-Pulia N et al. (2020) High-resolution pharyngeal manometry and impedance: protocols and metrics-recommendations of a high-resolution pharyngeal manometry international working group. Dysphagia 35(2):281-295. https://doi.org/10.1007/s00455-019-10023-y.

16. Omari TI, Wiklendt L, Dinning P, Costa M, Rommel N, Cock C (2014) Upper esophageal sphincter mechanical states analysis: a novel methodology to describe UES relaxation and opening. Front Syst Neurosci. 8:241. https://doi.org/10.3389/fnysci.2014.00241.

17. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C (2016) PRESS peer review of electronic search strategies: 2015 guideline statement. J Clin Epidemiol 75:40-46. https://doi.org/10.1016/j.jclinepi.2016.01.021.

18. EndNote (2013). Endnote X9 ed. [software]. Philadelphia (PA): Clarivate.
35. Robison R, DiBiase L, Ashley A, McElheny K, Anderson A, Wymer JP, Plowman EK (2021) Swallowing Safety and Efficiency Impairment Profiles in Individuals with Amyotrophic Lateral Sclerosis. Dysphagia 19(3):177-186. https://doi.org/10.1007/s00455-019-10088-9.

36. Heslin N (2020) Alterations to pharyngo-esophageal pressures with effortful swallow in adults with dysphagia: a high-resolution manometry study. Paper presented at: The 10th European Society of Swallowing Disorders Virtual Congress; 2020 Oct 8–10. Dysphagia. Forthcoming

37. Cock C, Francis R, Doeltingen S, Omair T (2019) Clinical implications of upper esophageal sphincter restriction in motor neuron disease. Paper presented at: 30th MND Symposium; 2019 Dec 4–6. Amyotrophic Lateral Scler. 20(1); 327-347. https://doi.org/10.1080/21678421.2019.1647002

38. van Es MA, Hardiman O, Chio A, Al-Chalabi A, Pasterkamp RJ, Veldink JH, van den Berg LH (2017) Amyotrophic lateral sclerosis. Lancet 390(10107):2084-2098. https://doi.org/10.1016/s0140-6736(17)31287-4.

39. Marin B, Fontana A, Arcuti S, Copetti M, Boumédiene F, Couratier P, Beghi E, Preux PM, Logroscino G (2018) Age-specific ALS incidence: a dose–response meta-analysis. Eur J Epidemiol 33(7):621-634. https://doi.org/10.1007/s10654-018-0392-x.

40. Winiker K, Gillman A, Guiu Hernandez E, Huckabee ML, Gozdzikowska K (2018) A systematic review of current methodology of high resolution pharyngeal manometry with and without impedance. Eur Arch Otorhinolaryngol 276(3):631-645. https://doi.org/10.1007/s00405-018-5240-9.

41. Rogus-Pulia, NM, Jones, CA, Forgues, AL, Orne, J, Macdonald, CL, Connor, NP & McCulloch, TM (2020) Perceived professional and institutional factors influencing clinical adoption of pharyngeal high-resolution manometry. Am J Speech Lang Pathol 29(3), 1550-1562. https://doi.org/10.1044/2020_AJSLP-19-00134.

42. Knigge M, Marvin S, Thibeault S (2018) Safety and tolerability of pharyngeal high-resolution manometry. Am J Speech Lang Pathol 28(1);43-52. https://doi.org/10.1044/2018_AJSLP-18-0039.

43. Leder SB, Novella S, Patwa H (2004) Use of fiberoptic endoscopic evaluation of swallowing (FEES) in patients with amyotrophic lateral sclerosis. Dysphagia 19(3):177-181. https://doi.org/10.1007/s00455-004-0009-2.

44. Fattori B, Siciliano G, Mancini V, Bastiani L, Bongioanni P, Caldarazzo Ienco E, Barillari M, Romeo SO, Nacci A (2017) Dysphagia in amyotrophic lateral sclerosis: relationships between disease progression and fiberoptic endoscopic evaluation of swallowing. Auris Nasus Larynx 44(3):306-312. https://doi.org/10.1016/j.anl.2016.07.002.

45. Loizou L, Small M, Dalton G (1980) Cricopharyngeal myotomy in motor neuron disease. J. Neurol. Neurosurg. Psychiatry 43:42-5. https://doi.org/10.1136/jnnp.43.1.42.

46. Waito AA, Tabor-Gray LC, Steele CM, Plowman EK (2018) Reduced pharyngeal constriction is associated with impaired swallowing efficiency in amyotrophic lateral sclerosis (ALS). Neurogastroenterol Motil 30(12). https://doi.org/10.1111/nmo.13450.

47. Robison R, DiBiase L, Ashley A, McElheny K, Anderson A, Wymer JP, Plowman EK (2021) Swallowing Safety and Efficiency Impairment Profiles in Individuals with Amyotrophic Lateral Sclerosis. Dysphagia 1-11. https://doi.org/10.1007/s00455-021-10315-2

48. Tabor-Gray L, Vasilopoulos T, Plowman EK (2020) Differences in voluntary and reflexive cough strength in individuals with amyotrophic lateral sclerosis and healthy adults. Muscle & Nerve 62(5): 597-600. https://doi.org/10.1002/mus.27040
Appendices:

**Database search strings.**

**PubMed Search:** In text: 35 results

**CINAHL search:**

(TI (deglutition* OR swallow* OR oropharyngeal OR pharyn* OR dysphagi* OR feed* OR fed OR eat OR eating OR eats OR ate OR drink* OR drank) OR AB (deglutition* OR swallow* OR oropharyngeal OR pharyn* OR dysphagi* OR feed* OR fed OR eat OR eating OR eats OR ate OR drink* OR drank) OR (MH "Deglutition") OR (MH "Deglutition Disorders") ) AND (TI ("motor neurone disease*" OR "motor neuron disease*" OR MND OR ALS OR "motor system disease*" OR "anterior horn cell disease*" OR "lateral sclerosis" OR "lateral sclerosis" OR "progressive bulbar palsy" OR "bulbar paralysis" OR "progressive muscular atroph*" OR "charcot disease*" OR "Lou Gehrig" OR "mixed etiolog*" OR "mixed aetiolog*") OR AB ("motor neurone disease*" OR "motor neuron disease*" OR MND OR ALS OR "motor system disease*" OR "anterior horn cell disease*" OR "lateral sclerosis" OR "lateral sclerosis" OR "progressive bulbar palsy" OR "bulbar paralysis" OR "progressive muscular atroph*" OR "charcot disease*" OR "Lou Gehrig" OR "mixed etiolog*" OR "mixed aetiolog*") OR (MH "Motor Neuron Diseases") ) AND (TI (manometry OR high resolution OR "pharyngeal pressure*") OR AB (manometry OR high resolution OR "pharyngeal pressure*") OR (MH "Manometry"))

**Limiters:** Exclude Medline records: 1 result

**EMBASE search:**

(deglutition*:ab,ti OR swallow*:ab,ti OR oropharyngeal:ab,ti OR pharyn*:ab,ti OR dysphagi*:ab,ti OR feed*:ab,ti OR fed:ab,ti OR eat:ab,ti OR eating:ab,ti OR eats:ab,ti OR ate:ab,ti OR drink*:ab,ti OR drank:ab,ti OR 'swallowing'/exp OR 'dysphagia'/exp) AND ("motor neurone disease*":ab,ti OR 'motor neurone disease*':ab,ti OR MND:ab,ti OR ALS:ab,ti OR 'motor system disease*':ab,ti OR 'anterior horn cell disease*':ab,ti OR 'lateral sclerosis':ab,ti OR 'lateral sclerosis':ab,ti OR 'progressive bulbar palsy':ab,ti OR 'bulbar paralysis':ab,ti OR 'progressive muscular atroph*':ab,ti OR 'charcot disease*':ab,ti OR 'lou gehrig':ab,ti OR 'mixed etiolog*':ab,ti OR 'mixed aetiolog*':ab,ti OR 'motor neuron disease'/exp) AND (manometry:ab,ti OR 'high resolution':ab,ti OR 'pharyngeal pressure*:ab,ti OR 'manometry'/exp)

**Limiter:** Exclude Medline record: 22 results

**Web Of Science Core search:**

**TOPIC:** (deglutition* OR swallow* OR oropharyngeal OR pharyn* OR dysphagi* OR feed* OR fed OR eat OR eating OR eats OR ate OR drink* OR drank) AND **TOPIC:** ("motor neurone disease*" OR "motor neuron disease*" OR MND OR ALS OR "motor system disease*" OR "anterior horn cell disease*" OR "lateral sclerosis" OR "lateral sclerosis" OR "progressive bulbar palsy" OR "bulbar paralysis" OR "progressive muscular atroph*" OR "charcot disease*" OR "Lou Gehrig" OR "mixed etiolog*" OR "mixed aetiolog*") AND **TOPIC:** (manometry OR high resolution OR "pharyngeal pressure*")

No Limits: 56 results
Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

| SECTION          | ITEM | PRISMA-ScR CHECKLIST ITEM                                                                 | REPORTED ON PAGE # |
|------------------|------|-------------------------------------------------------------------------------------------|--------------------|
| TITLE            | Title| Identify the report as a scoping review.                                                    |                    |
| ABSTRACT         | Structured summary | Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives. |                    |
| INTRODUCTION     | Rationale | Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach. |                    |
|                  | Objectives | Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives. |                    |
| METHODS          | Protocol and registration | Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address), and if available, provide registration information, including the registration number. |                    |
|                  | Eligibility criteria | Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale. |                    |
|                  | Information sources* | Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed. |                    |
|                  | Search | Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated. |                    |
|                  | Selection of sources of evidence† | State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review. |                    |
|                  | Data charting process‡ | Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators. |                    |
|                  | Data items | List and define all variables for which data were sought and any assumptions and simplifications made. |                    |
|                  | Critical appraisal of individual sources of evidence§ | If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate). |                    |
|                  | Synthesis of results | Describe the methods of handling and summarizing the data that were charted. |                    |
| SECTION                        | ITEM | PRISMA-ScR CHECKLIST ITEM | REPORTED ON PAGE # |
|--------------------------------|------|---------------------------|--------------------|
| RESULTS                        |      |                           |                    |
| Selection of sources of evidence | 14   | Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram. |                    |
| Characteristics of sources of evidence | 15   | For each source of evidence, present characteristics for which data were charted and provide the citations. |                    |
| Critical appraisal within sources of evidence | 16   | If done, present data on critical appraisal of included sources of evidence (see item 12). |                    |
| Results of individual sources of evidence | 17   | For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives. |                    |
| Synthesis of results           | 18   | Summarize and/or present the charting results as they relate to the review questions and objectives. |                    |
| DISCUSSION                     |      |                           |                    |
| Summary of evidence            | 19   | Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups. |                    |
| Limitations                    | 20   | Discuss the limitations of the scoping review process. |                    |
| Conclusions                    | 21   | Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps. |                    |
| FUNDING                        |      |                           |                    |
| Funding                        | 22   | Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review. |                    |

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where sources of evidence (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.
† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with information sources (see first footnote).
‡ The frameworks by Arksey and O'Malley (5) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.
§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of “risk of bias” (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2016;169:467–473. doi: 10.7326/M16-0850.
| Study            | Number Pts | Gender          | Age       | MND Classification | MND severity | Time since MND diagnosis | Dysphagia severity                  |
|------------------|------------|-----------------|-----------|--------------------|--------------|--------------------------|-------------------------------------|
| Takasaki et al. 2010 | 1          | Male            | 60yrs    | NR                 | NR           | 1.5 yrs.                 | Descriptive: presented with intractable aspiration |
| Regan, 2020      | 2          | 1 Male 1 Female | 82yrs 78yrs | Bulbar onset       | NR           | NR                      | FOIS score: 4                         |
|                  |            |                 |           |                    |              |                          | FOIS score: 3                         |
| Heslin, 2020     | 2          | 1 Male 1 Female | 82yrs 78yrs | Bulbar onset       | NR           | NR                      | FOIS score: 4                         |
|                  |            |                 |           |                    |              |                          | FOIS score: 3                         |
| Suh et al., 2019 | 41         | 21 Male 20 Female | 65±11yrs | NR                 | NR           | NR                      | FOIS 1 group FOIS 2/3 group FOIS4/7 group (Demographics of groups NR) |
| Cock et al., 2019| 16         | 8 Male 8 Female | 70±8yrs  | Bulbar group Pseudobulbar group (Demographics of groups NR) | NR (Abstract) | NR (Abstract) | NR (Abstract) |
| Cock et al., 2015| 16         | 10 Male 6 Female | 70±9yrs  | Lower MN involvement (11pts) Upper MN involvement (5pts) | NR           | NR          | Descriptive: All Pts had moderate-severe dysphagia; none were tube fed |

FOIS: functional oral intake scale; MN: motor neurone; NR: not reported; Pts: participants; yrs: year.
### Table 2. PHRM protocol and analysis methods.

| Study          | PHRM Equipment                                                                 | Data Acquisition                                                                 | Data Analysis               |
|----------------|--------------------------------------------------------------------------------|---------------------------------------------------------------------------------|-----------------------------|
| Takasaki et al., 2010 | Mano Scan 36 pressure sensors; 1 cm 4.2mm Circumference Fasting NS Upright No 5 minutes Syringe 3 Dry swallow Dry swallows | Mano-View                                                                       |
| Regan, 2020    | Mano Scan 36 pressure sensors; 1 cm 4.2mm Circumference Fasting 4 hours Upright No 5 minutes Syringe 2 10ml Liquid Swallow Gateway |                                                             |
| Heslin, 2020   | Mano Scan 36 pressure sensors; 1 cm 4.2mm Circumference Fasting 4 hours Upright No 5 minutes Syringe 2 10ml Liquid Swallow Gateway |                                                             |
| Suh et al., 2019 | InSight 36 pressure sensors; 1 cm but 2 cm in 5 places Fasting NS Upright Food-4 hours Drink-2 hours Neutral head position Yes 5-10 minutes NR 2 5ml Water Bio View Analysis |                                                             |
| Cock et al., 2019 | MMS Solar 36 Pressure sensors; 1 cm 16 impedance sensors; 2 cm Fasting NR (Abstract) Upright NR (Abstract) Neutral head position Yes 5-10 minutes NR (Abstract) 2 5ml Normal Saline MATLAB Algorithm |                                                             |
| Cock et al., 2015 | MMS Solar | 36 pressure sensors; 1cm & 16 impedance sensors; 2cm OR 25 pressure sensors; 1cm & 12 impedance sensors; 2cm | NR | Unidirectional | NR | Upright | Yes | 15minutes | Syringe | 5 | 5ml | Normal Saline | MATLAB algorithm |
|-----------------|-----------|-----------------------------------------------------------------|-----|----------------|-----|---------|-----|-----------|---------|----|-----|---------------|-----------------|

cm: centimetre; No: number; mm: millimetre; ml: millilitre; NR: not reported; Pt: participant.
| Study                  | Metric                                      | Definition of Metric reported | Subgroup of PwMND | Result                                      | Normative data | Statistical Values       |
|-----------------------|---------------------------------------------|--------------------------------|--------------------|---------------------------------------------|----------------|--------------------------|
| **Velopharynx**       |                                             |                                |                    |                                             |                |                          |
|                      |                                             |                                |                    |                                             |                |                          |
| Suh et al., 2019      | Velopharyngeal Pressure (mmHg)              | NR                             | FOIS1: FOIS2/3: FOIS4/7: | 137±34.31 146.13±35.75 213.46±62.29       | 208.88±94.4 | NR                       |
| Takasaki et al., 2010 | Dry pressure in velopharyngeal Muscle Zone (mmHg) | NR                             | 1Pt                | 95                                          | 141.1±73.5 | Maximum value            |
| Regan, 2020           | Velopharyngeal contractile integral (mmHg.cm.s) | Measure of contractile vigour within the velopharyngeal region only | FOIS3: FOIS4:     | 58.84±13.97 36.155±2.57                     | NR            | Mean & Standard deviation |
| Heslin, 2020          | Velopharyngeal Contractile integral (mmHg.cm.s) | Measure of contractile vigour within the velopharyngeal region only | FOIS 3: FOIS4:     | 14.9 14.91                                  | NR            | Median                   |
| Suh et al., 2019      | Area integral of Velopharynx (mmHg.s)       | NR                             | FOIS1: FOIS2/3: FOIS4/7: | 35.5±19.10 39.30±35.01 52.30±26.60         | 54.99±35.37 | NR                       |
| **Mesopharynx**       |                                             |                                |                    |                                             |                |                          |
|                       |                                             |                                |                    |                                             |                |                          |
| Suh et al., 2019      | Pressure of tongue base (mmHg)              | NR                             | FOIS 1: FOIS2/3: FOIS4/7: | 101.09±20.24 99.10±58.9 120.14±31.00      | 144.4±28.6 | NR                       |
| Cock et al., 2019    | Tongue Base contractility (mmHg)            | NR                             | Pseudobulbar:      | 81±14                                       | 151±17        | NR (Abstract)            |
| Regan, 2020           | Mesopharyngeal contractile integral (mmHg.cm.s) | Measure of contractile vigour within mesopharyngeal region only | FOIS 3: FOIS4:     | 29.56±7.52 84.84±23.48                      | NR            | Mean & Standard deviation |
| Heslin, 2020          | Mesopharyngeal contractile integral (mmHg.cm.s) | Measure of contractile vigour within mesopharyngeal region only | FOIS 3: FOIS4:     | 39.86 37.52                                  | NR            | Median                   |
| Suh et al., 2019      | Area integral of tongue base (mmHg.s)       | NR                             | FOIS 1: FOIS2/3: FOIS4/7: | 45.70±12.30 45.85±33.28 48.56±24.20         | 54.67±18.65 | NR                       |
| **Hypopharynx**       |                                             |                                |                    |                                             |                |                          |
|                       |                                             |                                |                    |                                             |                |                          |
| Study, Year | Measurement Description | Measure Type | Data Range | Controls | Median & Interquartile ranges |
|------------|--------------------------|--------------|------------|----------|-----------------------------|
| Cock et al., 2015 | Hypopharyngeal intrabolus pressure (mmHg) | NR | MND Group: 13(7.6;21.5) | Aged controls: 8.9(4.2;17.9) Young controls: 8(3.4;13.6) |
| Suh et al., 2019 | Pressure of low pharynx (mmHg) | NR | FOIS1: 177.01±97.69 FOIS2/3: 280.45±98.03 FOIS4/7: 351.89±174.74 | NR |
| Suh et al., 2019 | Pressure of Pre-UES (mmHg) | NR | FOIS1: 123.03±59.9 FOIS2/3: 140.29±82.40 FOIS4/7: 149.41±57.52 | NR |
| Regan, 2020 | Hypopharyngeal contractile integral (mmHg.cm.s) | Measure of contractile vigour within hypopharyngeal region only | FOIS3: 103.245±35.67 FOIS4: 99.73±25.72 | NR |
| Heslin, 2020 | Hypopharyngeal contractile integral (mmHg.cm.s) | Measure of contractile vigour within hypopharyngeal region only | FOIS3: 110.02 FOIS4: 61.76 | NR |

**Global pharyngeal measures**

| Study, Year | Pharyngeal Peak Pressure (mmHg) | NR | MND Group: 77(57;118) | Aged controls: 161(117;221) Young controls: 136(104;208) |
|------------|---------------------------------|----|------------------------|-----------------------------|
| Regan, 2020 | Pharyngeal Contractile Integral (mmHg.cm.s) | Sum of pharyngeal pressure >20mmHg from superior pharyngeal constrictor margin to UES proximal margin over the period from UES opening to 0.5s after UES closure | FOIS3: 125.56±1.63 FOIS4 : 105.92±9.12 | NR |

**UES**

| Study, Year | Pharyngeal Contractile Integral (mmHg.cm.s) | Sum of pharyngeal pressures >20 mmHg from the velopharynx to the UES proximal margin over the period from UES opening to 0.5 s after UES closure. | FOIS3: 164.78 FOIS4: 114.19 | NR |

**UES Relaxation Time**

| | | | | |

---
| Source, Year | Measurement | Description | FOIS 3: | FOIS 4: | Mean & Standard deviation |
|--------------|-------------|-------------|---------|---------|--------------------------|
| Regan, 2020  | UES Relaxation Time (s) | A measure of duration of pressure drop at UES 50% below baseline or 35 mmHg | 0.88±0.001, 0.485±0.1 | NR | |
| Heslin, 2020 | UES Relaxation Time (s) | A measure of duration of pressure drop at UES 50% below baseline or 35 mmHg | 0.6, 0.68 | NR | Median |
| UES Integrated Relaxation Pressure | UES Integrated Relaxation Pressure (mmHg) | A measure of the extent of UES relaxation – median of the lowest non-consecutive 0.20 – 0.25 s of pressure | 12.19±0.13, 0.235±6.89 | NR | Mean & Standard deviation |
| Regan, 2020  | UES Integrated Relaxation Pressure (mmHg) | A measure of the extent of UES relaxation – median of the lowest non-consecutive 0.20 – 0.25 s of pressure | 6.49, 4.8 | NR | Median |
| Cock et al., 2019 | UES Integrated Relaxation Pressure (mmHg) | NR (Abstract) | 6.1±2.7, 0.3±1.1 | NR | |
| Cock et al., 2015 | UES Integrated Relaxation Pressure 2.0 (mmHg) | Median of the lowest pressures recorded over 0.2 cumulative, but not necessarily consecutive seconds. | 3.6(0.7;6.9) | MND Group: 3.6(0.7;6.9) | Aged controls: 3.6(-0.2;8.7) Young controls: 3.6(-3;2.3) |
| Suh et al., 2019 | Pressure of minimal UES (mmHg) | NR | 1.65±15.01, 7.33±5.47, 10.02±4.37 | -7.97±5.64 | NR |
| UES Maximum Admittance | UES Max Admittance (mS) | Highest level of UES admittance reached during relaxation. | 2.7(2.5;3.4) | MND Group | Aged controls: 4.3(3.5;5.6) Young controls: 5.6(4.7;6.3) |
| Cock et al., 2019 | ‘Evidence UES restriction’(mS) | NR (Abstract) | Bulbar: 3.7±0.4, 4.1±0.3 | 7±0.5 | NR |
| UES Basal Pressure | | | | | |
| Study                        | Measure                                      | Definition                                                                 | FOIS:          | Value                     | Standard deviation | Note   |
|------------------------------|----------------------------------------------|---------------------------------------------------------------------------|---------------|---------------------------|--------------------|--------|
| Regan, 2020                  | UES Basal Pressure (mmHg)                    | Pre-swallow basal pressure in UES defined as average UES profile pressure recorded over the period from 1 to 0.25 s prior to UES opening | FOIS3:        | 61.02±1.05                | 29.79±10.35        | NR     |
|                              |                                              |                                                                           | FOIS4:        | 29.79±10.35               |                    |        |
| Cock et al., 2019            | UES Baseline tone (mmHg)                     | NR (Abstract)                                                             | Bulbar:       | 12±4                      | 35±5               | NR     |
|                              |                                              |                                                                           | Pseudobulbar: | 12±4                      | 35±5               |        |
| Takasaki et al., 2010        | Resting UES pressure (mmHg)                  | NR                                                                        | 1Pt           | 89                        |                    | Maximum|
| Regan, 2020                  | UES Peak Pressure (mmHg)                     | UES post-relaxation peak pressure defined as maximum UES profile pressure recorded from 0 to 1 s after UES closure | FOIS3:        | 222.145±2.8               | 280.36±19.79       | NR     |
|                              |                                              |                                                                           | FOIS4:        | 222.145±2.8               | 280.36±19.79       |        |
| Takasaki et al., 2010        | UES Zone (mmHg)                              | NR                                                                        | 1Pt           | 172.7±73.8                |                    | Maximum|
| Suh et al., 2019             | Pressure of cricopharyngeus (mmHg)           | NR                                                                        | FOIS 1:       | 181.4±107.91              |                    | NR     |
|                              |                                              |                                                                           | FOIS2/3:      | 200.90±89.95              |                    |        |
|                              |                                              |                                                                           | FOIS4/7       | 247.52±78.85              |                    |        |
|                              |                                              |                                                                           | 388.2±137.21  | 200.90±89.95              |                    |        |

cm: centimetre; FOIS: functional oral intake scale; mmHg: unit of pressure; NR: not reported; Pt: participant; s: second.
Table 4. Effects of intervention.

| Study | Intervention | Intervention description | Metric | Baseline | Post intervention |
|-------|--------------|--------------------------|--------|----------|-------------------|
| Alteration in bolus characteristics | | | | | |
| Sensory Stimulation | | | | | |
| Regan, 2020 | Sensory stimulation | Duplicate 10ml neutral (still water), sour (Lemon juice), cold (still water 3-5 degrees) and carbonated (Sparkling liquid) swallows given to participants in randomized order. | Velopharyngeal Contractile Integral (mmHg.cm.s) | 58.84±13.97 | Cold: 96.88±10.73 Sour: 93.89±0.46 Carbon: 107.69±5.08 |
| | | | Mesopharyngeal Contractile Integral (mmHg.cm.s) | 29.56±7.52 | Cold: 43.68±9.37 Sour: 75.66±43.47 Carbon: 127.83±3.6 |
| | | | Hypopharyngeal Contractile Integral (mmHg.cm.s) | 103.24±35.67 | Cold: 101.88±18.63 Sour: 104.57±30.14 Carbon: 134.92±55.18 |
| | | | Pharyngeal Contractile Integral (mmHg.cm.s) | 125.56±1.63 | Cold: 187.6±10.52 Sour: 189.7±7.92 Carbon: 213.9±49.5 |
| | | | UES Relaxation Time (s) | 0.88±0.001 | Cold: 0.67±0.08 Sour: 0.875±0.39 Carbon: 0.785±0.16 |
| | | | UES Integrated Relaxation Pressure (mmHg) | 12.19±0.13 | Cold: 6.17±10.52 Sour: 14.66±2.51 Carbon: 5.44±2.65 |
| | | | UES Basal Pressure (mmHg) | 61.02±1.05 | Cold: 48.78±6.38 Sour: 60.69±0.06 Carbon: 84.64±50.79 |
| | | | UES Peak Pressure (mmHg) | 222.145±2.8 | Cold: 127.38±19.37 Sour: |
| Change in bolus consistency | Liquid bolus | Viscous bolus |
|-----------------------------|-------------|---------------|
| **Cock et al., 2015** | Altering bolus consistency | Participants given 5ML liquid (0.9% normal saline) and 5ML Viscous bolus (Viscous Swallow Challenge Medium) | Pharyngeal Peak Pressure (mmHg) | 77(57;118) | 69(64;109) |
| | | | Hypopharyngeal intrabolus pressure (mmHg) | 13(7.6;21.5) | 18.7(12.3;24.1) |
| | | | UES Integrated Relaxation Pressure 0.2 (mmHg) | 3.6(0.7;6.9) | 6.9(3.8;13.6) |
| | | | UES Maximum Admittance (mS) | 2.7(2.5;3.4) | 2.9(2.3;3.3) |

| Swallowing manoeuvres | Effortful swallow | Normal Swallow | Effortful Swallow |
|-----------------------|------------------|---------------|------------------|
| **Heslin, 2020** | Effortful swallow | Participants complete a normal swallow and then told to swallow and “Squeeze hard with all of your muscles” | Velopharyngeal Contractile Integral (mmHg cm s) | P1: 14.9 | 9.5 |
| | | | P2: 14.91 | 59.89 |
| | | | Mesopharyngeal Contractile Integral (mmHg cm s) | P1: 39.86 | 27.48 |
| | | | P2: 37.52 | 43.34 |
| | | | Hypopharyngeal Contractile Integral (mmHg cm s) | P1: 110.02 | 59.19 |
| | | | P2: 61.76 | 38.77 |
| | | | Pharyngeal Contractile Integral (mmHg cm s) | P1: 164.78 | 75.75 |
| | | | P2: 114.19 | 162.43 |
| | | | UES Relaxation Time (s) | P1: 0.6 | 1.01 |
| | | | P2: 0.68 | 0.8 |
| | | | UES Integrated Relaxation Pressure (mmHg) | P1: 6.49 | 0.37 |
| | | | P2: 4.8 | 12 |

| Surgical | Cricopharyngeal myotomy | Prior Myotomy | Post Myotomy |
|----------|-------------------------|---------------|--------------|
| **Takasaki et al., 2010** | Cricopharyngeal myotomy | Bilateral cricopharyngeal myotomy | Resting UES pressure (mmHg) | 89 | 21 |
|                         | Dry swallowing pressure in the velopharyngeal muscle zone (mmHg) | 95 | 96 |
|-------------------------|---------------------------------------------------------------|----|----|
|                         | UES Zone (mmHg)                                               | 171| 75 |

cm: centimetre; FOIS: functional oral intake scale; mmHg: unit of pressure; P1: participant 1; P2: participant 2; s: second.
**Figure Legend:**

**Fig 1** Prisma 2009 Flow Diagram

**Fig 2** Pharyngeal metric sites and measurement parameters reported across studies and percentage of studies documenting each

**Fig 3** Upper oesophageal sphincter (UES) measurement parameters reported across studies and percentage of studies documenting each

**Fig 4** Pharyngeal metric data in healthy participants (red shades) vs PwMND (blue shades). PwMND and healthy participants are sub-grouped as per study e.g., FOIS 1, FOIS2/3 FOIS4/7 all PwMND but grouped according to FOIS severity as in the study of Suh et al., 2019

**Fig 5** UES Metric data in Healthy Participants (shades of red) vs PwMND (shades of blue). Similarly as seen in Figure 4 PwMND and healthy participants are sub grouped as per study
Fig1.
**Fig 2.**
UES Integrated Relaxation pressure (IRP): 83%
UES IRP: 50%
UES IRG 0.2: 17%
Pressure of minimal UES: 16.6%
No Data: 50%

UES Basal Pressure: 50%
UES Basal pressure: 17%
UES Baseline tone: 17%
Resting UES pressure: 17%
No Data: 50%

UES Relaxation Time (RT): 33%
UES RT: 33%
No Data: 67%

UES Peak Pressure (Peak P): 50%
UES Peak P: 17%
Pressure in UES Zone: 17%
Pressure of Cricopharyngeus: 17%
No data: 50%

UES Max Admittance: 33%
UES Max Admittance: 17%
Evidence of UES restriction: 17%
No Data: 67%

Fig. 3
Fig 4.
Fig 5.