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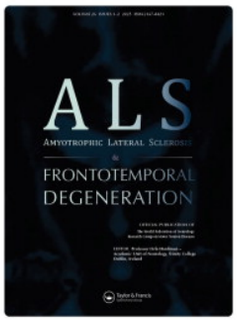

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Further development of a patient-reported outcome measure to assess the impact of oral secretion problems in people living with MND

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RESEARCH ARTICLE

Further development of a patient-reported outcome measure to assess the impact of oral secretion problems in people living with MND

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Abstract

Objective: Oral secretion problems are common yet poorly managed in people living with MND (plwMND). A validated patient-reported outcome for measuring saliva symptoms in this patient group would facilitate better monitoring of individuals. This study aimed to assess the validity, reliability and sensitivity to change of a revised version of the clinical saliva score for MND (CSS-MNDr). *Methods:* Data were collected as part of a longitudinal, observational saliva management study. The CSS-MNDr, ALS Functional Rating Scale, a Global Rating of Change questionnaire and saliva-specific modified Likert scale were completed at each study visit, each of which probed the severity of saliva symptoms. Construct validity, test-retest reliability and sensitivity of the CSS-MNDr were assessed and the minimal important difference of the instrument was estimated. *Results:* The CSS-MNDr showed excellent test-retest reliability (intraclass correlation coefficient >0.9). Construct validity showed the CSS-MNDr performed as expected, with bulbar-onset participants scoring significantly higher than those who reported limb-onset across all visits (group mean scores). Strong correlation of total scores with the ALSFRS-R saliva question was demonstrated (-0.8), with the thick subscore correlating less well (-0.5). A minimal important difference in the range of -2.5 to -3.6 over 3 months was estimated for worsening symptoms. *Conclusions:* The CSS-MNDr has been validated as a reliable patient reported outcome for measuring saliva problems in plwMND. With separate scores for thick and thin secretion problems, the CSS-MNDr is the most comprehensive tool for assessing salivary problems in plwMND reported to date.

Keywords: *Motor neuron disease, MND, amyotrophic lateral sclerosis, ALS, sialorrhea, saliva, secretion management*

Introduction

Motor neuron disease (MND) is a devastating neurodegenerative disorder, characterized by the progressive loss of motor functions. Despite determined research efforts, a cure remains elusive, with current treatments only offering a modest improvement in life expectancy (1–3). Therefore, management of MND is focussed on minimizing symptoms associated with the disease in an effort to improve quality of life.

People living with MND (plwMND) commonly suffer from problems with oral secretions believed due to declining capacity to swallow rather than increased production of fluids. Inability to clear saliva or mucus from the mouth can lead to sialorrhea (drooling) or aspiration into the lungs. These can in turn lead to skin irritation around the mouth, feelings of social anxiety, difficulties in using non-invasive ventilation (NIV, a critical component of later-stage care), coughing, struggling to clear fluids from the lungs and lung infections (4,5).

To facilitate comparisons of interventions for secretion issues in plwMND, reliable, validated tools for measuring the extent of problems are essential. Objective measures of saliva production have been trialled, but suffer from practicality and poor correlation

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with patient perception of severity issues (6). Previously, studies have reported use of a generic Sialorrhea Scoring Scale (SSS) tool (7,8), the MND-specific Oral Secretion Scale (OSS) (8–11) and Clinical Saliva Score for MND (CSS-MND) (6).

The OSS was developed for use with plwMND and asks an observer to select a score of 4–0 (normal – most severe) based on characteristics such as the frequency of drooling, frequency of pooling in the throat and how often oropharyngeal suctioning is required (9,11). The SSS was first used in a study testing glycopyrrolate to treat saliva problems in children with developmental disabilities and asked caregivers to rank the extent of drooling with a score from 1 to 9 (7). The OSS and SSS were tested in a French cohort of plwMND, which found both to have high inter- and intra-rater reliability (8). The study noted a limitation of the OSS in being restricted to 5 points, concluding the SSS is likely to be more sensitive when considering people with severe secretion problems. However, the only saliva score routinely included in studies involving plwMND is question 2 of the revised ALS functional rating scale (ALSFRS-R), which is similar to the OSS in scoring from 4-0 and focuses on thin secretions. None of these (OSS, SSS, ALSFRS-R question 2) consider thick secretions and all require a single score estimate, rather than asking varied questions.

The clinical saliva score for MND (CSS-MND) is a patient-reported outcome which aims to measure the underlying single attribute or construct of symptoms (impairments) and other aspects of wellbeing related to the effect of saliva problems in plwMND. The questionnaire assesses multiple aspects of secretion problems, e.g. considering day- and nighttime issues separately and querying the social impact of these symptoms, alongside questions relating to drooling frequency and impact on NIV usage. The tool has been shown to be acceptable and easy to use (6). The CSS-MND offers a better reflection of the saliva burden compared to a single question-based scale and could provide detailed analyses of different management options and their impacts. However, some revisions were suggested in the original study, including splitting the questionnaire into two domains focusing on thick (mucoidal) and thin (serous) saliva problems separately (6).

The aim of this study was to assess the validity, reliability and sensitivity to change of a revised version of the CSS-MND (CSS-MNDr) in a cohort of patients living with MND.

Materials and methods

ProSec3 study

ProSec3 was a prospective, observational, longitudinal study run across 34 sites in the UK (plus 1 in Australia) between February 2018 and September 2020. The main aim of the study was to describe the incidence of thin and thick secretion problems in the MND population of the UK. Adults with the following MND diagnoses were eligible to take part: amyotrophic lateral sclerosis (ALS), primary lateral sclerosis (PLS), progressive muscular atrophy (PMA) and progressive bulbar palsy (PBP).

Participants completed up to 5 study visits aligned with their clinical care (intervals of approximately 3 months, Supplementary Table 1). The revised ALS functional rating scale (ALSFRS-R) (12), revised clinical saliva score for MND (CSS-MNDr), a modified Likert scale (MLS) and global rating of change questionnaire (GRoC) were completed at each visit (Supplementary Data). The CSS-MNDr, GRoC and MLS were completed by the participants, whereas the ALSFRS-R was completed via interview by a research team member in the majority of cases (98.7%, only 15 reported as self-completed).

A subset of participants who reported that their symptoms were stable ('about the same' on the GRoC) with no new saliva treatments recommended at visit 1 were asked to complete the CSS-MNDr, GRoC and MLS again approximately 1 week later. These data were collected to estimate the test-retest reliability of the CSS-MNDr (reliability arm).

This study was approved by the South Central-Hampshire B Research Ethics Committee (ref: 18/SC/0031) and informed consent was recorded prior to participation.

CSS-MNDr

The CSS-MNDr is a ten-item patient reported outcome measure. Response options differ between items but are based on a scale starting at zero (no saliva related problem) increasing to three (the most severe symptom option). Two questions relate specifically to the effect excess saliva has on the use of breathing apparatus, both of which have a score of (0, 0, 1, 2, 3) with the first 0 corresponding to not using a breathing machine.

The overall score for a patient represents the sum of scores for each individual question and ranges from 0–30 with a higher number indicating greater problems with saliva. Patients who do not use a breathing machine score 0–24, as the questions relating to effects on use of such equipment are omitted. These scores are scaled up to 30 for comparison (transformed score). The standard operating procedure with details regarding the scoring system and recommendations for dealing with missing data are in the Supplementary Data.

Participants completed the CSS-MNDr based on their symptoms at the time of completion, regardless of any methods employed to manage secretions at that time.

ALSFRS-R (item/question 2)

The ALSFRS-R is validated for self-completion in person and over the telephone (13–15). The saliva

item has 5 responses ranging from 4 (no saliva problem/normal) to 0 (marked drooling; requires constant tissue or handkerchief).

Modified Likert Scale (MLS)

We used a 5-point Likert scale for responses to the question 'On a scale of 1–5, where 1 indicates no effect at all and 5 indicates a very severe effect, how would you rate the effects of saliva problems on your health in the last week?'

Global Rating of Change Questionnaire (GRoC)

A self-reported global rating of change questionnaire asked 'concerning your saliva and secretions, how much do you think your symptoms have changed in the last three months?' 5 responses: improved a great deal, improved a little, about the same (or never had a saliva/secretion problem), worsened a little, worsened a great deal. This question was used to assign individuals into the reliability arm.

Statistical analysis

All analyses were conducted using R version 4.4.1 (16).

We sought to assess the reliability, validity, sensitivity and responsiveness of the CSS-MNDr in this study. Construct validity (known group validity) was established by comparing CSS-MNDr scores across two groups split according to MND onset (limb versus bulbar onset). A two independent samples *t*-test was performed comparing mean CSS-MNDr scores between the two groups. A priori, we hypothesized a higher CSS-MNDr score in the bulbar onset group compared to the limb onset group. Additionally, we explored the correlation of both the ALSFRS-R secretion sub-score and the MLS with the CSS-MNDr to assess construct validity (convergent).

The test-retest reliability of the CSS-MNDr was tested using the intra-class correlation coefficient (ICC) (two-way model, single measure) with a 95% confidence interval (CI) at re-test for participants in the reliability arm. Excellent or good reliability is indicated by an ICC greater than 0.9 or between 0.75 and 0.9 respectively (17). Pearson's correlation was also calculated. Agreement was evaluated graphically by the Bland and Altman approach.

To assess the sensitivity to change of the CSS-MNDr, the standardized response mean (the mean change from baseline (visit 1) to visit 2 divided by the standard deviation of the change) was calculated for the three self-reported global rating of change groups at 3 months (better, no change, worse) from the GRoC. This was repeated for groups derived from the change in MLS outcome from baseline to 3 months. The analyses were repeated using the MLS data, which should be less susceptible to recall error than the GRoC as it asks participants to recall over a much shorter period of time (1 week instead of 3 months). As the MLS yielded a numerical response, participants were grouped based on whether their score had remained the same, increased or got smaller (indicating worsening or improvement of symptoms respectively). These analyses compare the CSS-MNDr score with patient perception of any change in their saliva symptoms. Mean changes in score between the three GRoC groups (same, better, worse) were compared with a one-way analysis of variance (ANOVA) model.

The sensitivity to change analysis was further used to estimate the minimal important difference of the CSS-MNDr. The GRoC, a self-reported rating of quality of life (specific to saliva issues), and the MLS were used as anchors in conjunction with the CSS-MNDr scores to estimate the minimal important difference (18).

Results

Demographics

Table 1 presents the ProSec3 study demographic data. The majority of participants had a diagnosis of ALS (81.8%), with a larger proportion reporting limb-onset than bulbar (67.6%). The cohort was predominantly male (61.6%).

CSS-MNDr score summary

Table 2 presents summary statistics for the CSS-MNDr overall score at each clinical visit and for the reliability arm.

CSS-MNDr validity

Construct validity (known group validity). To test the known group construct validity we conducted a two independent sample t-test (limb versus bulbar onset) with the hypothesis that the CSS-MNDr score in the bulbar onset group would be higher than the limb onset group. The results are presented in Table 3.For all 5 clinical visits the bulbar onset group had a higher mean CSS-MNDr than the limb onset group.

Construct validity (convergent). To assess the convergent construct validity we explored the correlation of both the ALSFRS-R secretion sub score (item/question 2) and the MLS with the overall CSS-MNDr score (and individual items) (Table 4).

The Pearson correlation coefficients for the overall CSS-MNDr score with (a) the ALSFRS-R secretion sub score (item 2) and (b) the MLS were −0.8 and 0.7, respectively. The correlations between each of the items on the CSS-MNDr were also analysed. The individual items' correlation coefficients with the ALSFRS-R secretion sub score ranged from −0.3 to −0.8.

Table 1. Key characteristics of the study population.

	ProSec 3 population ($N = 479$)	
Characteristic	Mean (SD)	Median (IQR)
Age	64.45 (10.93)	66 (57–73)
	N	%
Sex		
Male	295	61.6
Female	176	36.7
Missing	8	1.7
Ethnicity		
White	456	95.2
Other	22	4.6
Missing	1	0.2
MND onset type		
Familial	30	6.3
Sporadic	443	92.5
Missing	6	1.3
MND onset site		
Bulbar	127	26.5
Limb	324	67.6
Other	25	5.2
Missing	3	0.6
MND diagnosis criteria		
ALS	392	81.8
Not ALS (Other)*	81	16.9
MND (unspecified)	3	0.6
Missing	3	0.6

*Refers to diagnoses of MND other than ALS i.e., PLS, PMA and PBP.

Table 2. Summary statistics for the revised version of the clinical saliva score for MND (CSS-MNDr) data grouped by study visit.

Visit	Mean	SD	Median	LQ	UQ	Min	Max	*N*
Clinical visit 1	7.6	7.4	6.2	0.0	13.8	0.0	28.8	462
Clinical visit 2	8.4	7.4	7.5	1.0	14.0	0.0	25.0	319
Clinical visit 3	7.7	7.3	6.0	0.0	13.0	0.0	25.0	213
Clinical visit 4	7.7	7.2	6.2	1.0	12.8	0.0	26.2	135
Clinical visit 5	8.0	7.3	6.2	1.4	12.5	0.0	28.8	82
Reliability arm	4.3	5.6	2.0	0.0	7.5	0.0	27.5	144

Relativity arm refers to the subset of participants who repeated the CSS-MNDr, global rating of change questionnaire (GRoC) and Modified Likert Scale (MLS) assessments 2–10 days after visit 1. Note that these figures report the centers and spread of data collected at each visit, but these are impacted by the decline in numbers of participants over the study visits.

Table 3. Data for the revised version of the clinical saliva score for MND (CSS-MNDr) were grouped by study visit and site of disease onset, with mean and standard deviation shown for each subgroup.

	Bulbar			Limb			Difference		
Visit	Mean	SD	*N*	Mean	SD	*N*	Mean	95% CI	
Clinical visit 1	13.6	6.9	120	5.3	6.2	315	8.3	6.9	9.8
Clinical visit 2	14.0	6.6	88	6.2	6.5	216	7.8	6.2	9.4
Clinical visit 3	13.9	7.0	56	5.4	6.1	147	8.4	6.3	10.6
Clinical visit 4	14.1	7.1	32	5.5	6.0	97	8.6	5.8	11.4
Clinical visit 5	14.5	7.1	19	5.9	6.3	61	8.6	4.9	12.4

Note that these figures report the centers and spread of data collected at each visit, but these are impacted by the decline in numbers of participants over the study visits.

The correlation between the CSS-MNDr thin saliva questions (Part A) and thick saliva questions (Part B) with the ALSFRS-R secretion sub score were −0.8 and −0.5, respectively. The CSS-MNDr total score and the thin subscore both correlated slightly more strongly with the ALSFRS-R secretion sub score than the MLS (both −0.8 compared to 0.7), whilst the thick subscore was slightly more strongly correlated to the MLS than the ALSFRS-R item 2 (correlation coefficients of 0.7 and −0.5, respectively).

Test-retest reliability

To assess the test-retest reliability of the CSS-MNDr we calculated the ICC for participants in the reliability arm. The ICC was estimated to be 0.92 (95% CI: 0.89, 0.95, $n = 105$) for all reliability arm respondents with stable symptoms at both baseline and retest who completed the second CSS-MNDr within 14 days of their 1st study visit (Pearson correlation 0.90).

The Bland-Altman plot for this data shows the mean difference between all measurements to be close to zero (Figure 1).

Sensitivity to change

To assess the sensitivity to change of the CSS-MNDr, the standardised response mean was calculated for the three self-reported GRoC groups at 3 months (better, no change, worse) and for groups derived from changes in the MLS.

Global Rating of Change Questionnaire (GRoC)

The mean CSS-MNDr score change between visits 1 and 2 associated with each of the three outcomes on the GRoC are as follows: better: 1.5, same: 0.1, worse: −2.5 (Table 5). Those scores represent the minimal important difference for a change that is perceivable to a person living with MND over the ∼3 month period. The standardized response mean values for each group were: better: 0.4, same: 0.0, worse: −0.5. The mean CSS-MNDr score for the group of individuals with stable symptoms is lower than for those who reported an improvement or worsening of their saliva symptoms (same: 5.2, better: 12.2, worse: 11.4).

Modified Likert Scale (MLS)

The mean CSS-MNDr score change between visits 1 and 2 associated with each of the three outcomes on the MLS are as follows: better: 0.8, same: −0.1, worse: −3.6 (Table 6). The standardized

Table 4. Pearson's correlation coefficients of the revised version of the clinical saliva score for MND (CSS-MNDr) individual items and the CSS-MNDr score, thin secretion subscore (part A), thick secretion subscore (part B), modified likert scale (MLS) and the revised ALS functional rating scale (ALSFRS-R) saliva score (item 2) and bulbar domain (items 1, 2 and 3).

	A	B	C	D	E	F	G	H	I	J	CSS-MNDr score	Part A	Part B	MLS	ALSFRS-R item 2	ALSFRS-R bulbar domain
A	1	0.8	0.7	0.4	0.7	0.6	0.3	0.4	0.4	0.3	0.8	0.9	0.5	0.6	−0.7	−0.7
B	–	1	0.8	0.4	0.7	0.5	0.5	0.4	0.3	0.5	0.9	0.9	0.5	0.6	−0.8	−0.7
C	–	–	1	0.3	0.7	0.5	0.4	0.5	0.4	0.4	0.8	0.8	0.5	0.6	−0.7	−0.7
D	–	–	–	1	0.3	0.3	0.3	0.2	0.2	0.3	0.5	0.5	0.2	0.3	−0.3	−0.2
E	–	–	–	–	1	0.5	0.5	0.5	0.4	0.5	0.8	0.8	0.5	0.6	−0.7	−0.7
F	–	–	–	–	–	1	0.4	0.4	0.4	0.5	0.7	0.7	0.4	0.6	−0.5	−0.5
G	–	–	–	–	–	–	1	0.4	0.3	0.7	0.6	0.6	0.5	0.5	−0.4	−0.4
H	–	–	–	–	–	–	–	1	0.7	0.6	0.7	0.5	0.9	0.6	−0.5	−0.6
I	–	–	–	–	–	–	–	–	1	0.5	0.6	0.4	0.9	0.5	−0.4	−0.5
J	–	–	–	–	–	–	–	–	–	1	0.7	0.6	0.7	0.6	−0.4	−0.5
CCS-MNDr Score	–	–	–	–	–	–	–	–	–	–	1	1	0.7	0.7	−0.8	−0.8
Part A	–	–	–	–	–	–	–	–	–	–	–	1	0.5	0.7	−0.8	−0.7
Part B	–	–	–	–	–	–	–	–	–	–	–	–	1	0.6	−0.5	−0.6
MLS	–	–	–	–	–	–	–	–	–	–	–	–	–	1	−0.6	−0.6
ALSFRS item 2	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1	0.9
ALSFRS-R bulbar domain	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1

response mean values for each group were: better: 0.1, same: 0.0, worse: −0.7. Those scores represent the minimal important difference for a change that is perceivable to a person living with MND over the ∼3 month period. The mean CSS-MNDr score for the group of individuals with stable symptoms is lower than for those who reported an improvement or worsening of their saliva symptoms (same: 6.1, better: 12.5, worse: 8.4).

Questionnaire response rates

The mean percentage of the CSS-MNDr completed ranged from 98.9 to 100% across all visits with no questions consistently omitted.

Discussion

Oral secretion problems are common in plwMND but management of these symptoms is suboptimal (19,20). For better care pathways to be developed, effective measures of the severity of saliva problems are needed, both to facilitate interventional trials and monitor the progress of individual patients.

We present a revised version of the clinical saliva score for MND (CSS-MNDr) based on recommendations from the original study (6). The wording of questions has been clarified to assess only problems relating to excess saliva, and two subsections separating thin and thick saliva issues have been created.

The analyses have shown that the CSS-MNDr has construct validity. Known group construct validity was tested using two independent sample *t*-tests with an a priori hypothesis that the bulbar onset group would score higher than the limb onset group. This was confirmed at all visits. Convergent construct validity was tested by exploring the correlation between the overall CSS-MNDr score and both the ALSFRS-R secretion subscore and MLS, which were found to be −0.8 (very strong) and 0.7 (moderate) respectively (21). These results suggest that the CSS-MNDr has convergent construct validity. It is worth noting that the correlations between the CSS-MNDr subscores and the ALSFRS-R saliva item were −0.8 (very strong) for the thin and −0.5 (fair) for the thick questions (Pearson's correlation coefficients). This suggests that the ALSFRS-R may not be sufficient to measure saliva problems in those who have thick saliva issues. Our results are comparable with those on the Sialorrhea Scoring Scale and Oral Secretion Scale, which were found in a study on 53 plwMND to have Spearman correlation coefficients with the ALSFRS-R bulbar domain score of −0.797 and 0.803, respectively ($p < 0.0001$ for both) (8). Correlation coefficients for the SSS and OSS with the ALSFRS-R salivation items were −0.909 and 0.931 respectively

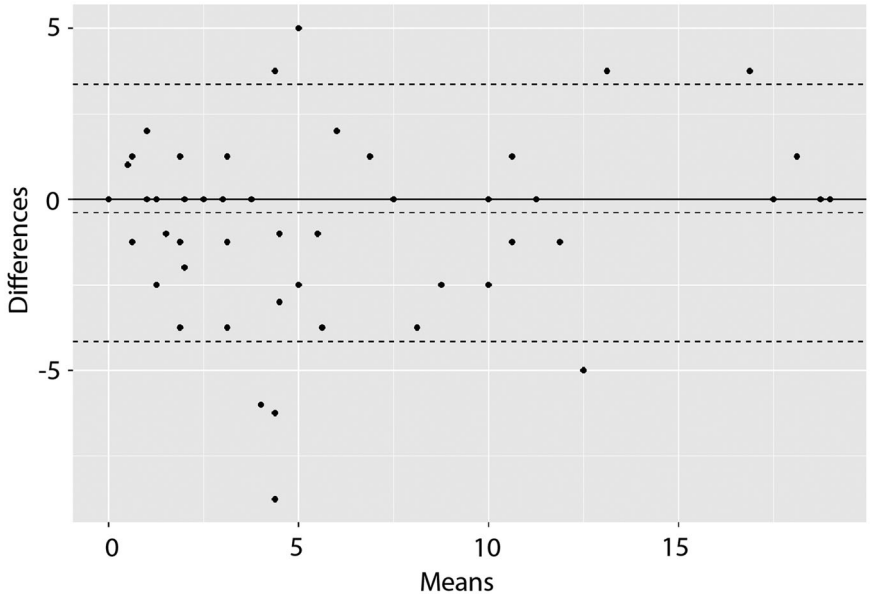

Figure 1. Bland-Altman plot for the test-retest group: revised clinical saliva score for MND (CSS-MNDr) data for all participants who reported stable symptoms both at visit 1 and when completing the retest, and who completed their retest within 14 days of their visit 1.

Table 5. Sensitivity to change results derived using the global rating of change (GRoC) data where participants reported how they felt their saliva and secretion symptoms had changed over the last three months.

Change	Mean visit 1	Mean visit 2	Mean change	SD	SRM	Mean monthly rate	SD	*N*
Better	12.2	10.7	1.5	3.6	0.4	0.66	1.39	19
Same	5.2	5.2	0.1	3.7	0.0	0.10	1.32	192
Worse	11.4	14.0	−2.5	5.5	−0.5	−0.90	2.32	97

Based on these outcomes at visit 2, participants were assigned to one of the following groups: 'better', 'same' and 'worse'. The values in the table refer to the revised version of the clinical saliva score for MND (CSS-MNDr) data collected for all the participants within each group. NB: 3 participants' data were removed due to invalid dates i.e., visit 2 dates earlier than visit 1. ANOVA comparing mean changes: $p = <0.001$.

Table 6. Sensitivity to change results derived using the Modified Likert Scale (MLS) where participants were asked to rate on a numerical scale the severity of the effects of saliva problems on their health in the last week.

Change	Mean visit 1	Mean visit 2	Mean change	SD	SRM	Mean monthly rate	SD	*N*
Better	12.5	11.7	0.8	5.9	0.1	0.41	2.14	51
Same	6.1	6.1	−0.1	3.2	0.0	0.03	1.00	193
Worse	8.4	12.0	−3.6	5.4	−0.7	−1.32	2.60	63

Based on these outcomes at visit 2, participants were assigned to one of the following groups: 'better', 'same', 'worse' depending upon whether their MLS score had changed (e.g. an increase in MLS score compared to visit 1 would indicate a worsening of symptoms). The values in the table refer to the revised version of the clinical saliva score for MND (CSS-MNDr) data collected for all the participants within each group. NB: 3 participants' data were removed due to invalid dates i.e., visit 2 dates earlier than visit 1. ANOVA comparing mean changes: $p = <0.001$.

($p < 0.0001$ for both). For direct comparison, Spearman rank correlation coefficients for the CSS-MNDr with the ALSFRS-R bulbar domain and ALSFRS-R saliva item were −0.788 and −0.793, respectively ($p = <0.001$). Whilst good correlation with the ALSFRS-R saliva and bulbar measures is desirable, incomplete correlation is also welcomed as an indicator that the CSS-MNDr is detecting some different aspect(s) of the symptom not already measurable by the widely collected ALSFRS-R data.

Test-retest reliability of the CSS-MNDr was assessed by calculating the ICC for those in the reliability arm. The ICC was over 0.9 which is considered indicative of excellent reliability (17) with a very strong Pearson correlation of 0.90

(21). The Bland-Altman plot revealed the mean of the differences between the two assessments to be very close to 0, indicating scores were not biased towards either time point. However, the scatter of data points is slightly greater towards the left of the plot indicating a possible proportional bias relative to the magnitude of the CSS-MNDr score.

Estimating the minimal important difference of the CSS-MNDr is essential in aiding the interpretation of score changes seen in plwMND. Using two quality of life scores as anchors, the GRoC and the MLS, minimal important differences over the ~3-month period between visits were calculated as −2.5 and −3.6 respectively for perception of a worsening of symptoms (between −0.90 and −1.32 points/month). Where people perceived improvement in saliva problems the minimal important differences were 1.5 and 0.8 (0.66 and 0.41 points/month). For each group, the two values can be considered a range between which the minimal important difference is believed to lie. Based on Cohen's thresholds, the standardised response means for the minimal important differences of the 'better' and 'worse' groups represent small and moderate sized effects respectively (22). The highly significant ($p < 0.001$) one-way ANOVA results suggest the CSS-MNDr is a sensitive instrument and can distinguish between the broad 'health' categories (better, worse, stable). Our methodology for estimating the minimal important difference means that the estimate is applicable to plwMND regardless of how far their symptoms have progressed. However, it may be of interest in the future to stratify individuals based on their point in the disease course and/or other characteristics such as site of MND onset. It is also of note that over 95% of our study participants were white. This is a limitation of all our reported findings which may not be representative of other groups and collecting data in the future to address this is desirable.

The CSS-MNDr had high percentages of completeness with no questions that were routinely left unanswered. This suggests that the participants felt the questions were acceptable.

The CSS-MNDr offers a number of advantages over the other question-based measures of saliva symptoms reported in previous studies on plwMND. Firstly, it separates thin and thick secretion problems into two domains, the scores of which can be considered separately. This is important, as treatments administered to reduce severity of serous secretions can exacerbate mucous secretion problems and vice versa. Secondly, the CSS-MNDr is scored out of a maximum of 30, potentially making it more sensitive to changes, particularly in people with very severe symptoms. Thirdly, the CSS-MNDr is the only saliva measure to consider the social impact of saliva problems and how oral secretions affect use of non-invasive ventilation (NIV). Lastly, as a validated patient-reported outcome measure (PROM), the CSS-MNDr could be incorporated into telehealth monitoring devices without further validation for self-completion. Whilst the PROM now measures more than just saliva problems, we opted to keep the original tool's name (clinical saliva score for MND) to acknowledge the critical role its predecessor played in the development of the CSS-MNDr. With its many features, the CSS-MNDr offers a comprehensive measure for the severity of oral secretions and how they impact the lives of plwMND.

Nonetheless, the CSS-MNDr is not without its limitations. The most prominent, and one shared with all the other measures, is lack of consideration of over-drying of the mouth. As dry mouth is a known side effect of some medications currently used in secretion management, it is important to consider this in any future interventional study, particularly as dysphagia accompanies secretion problems in plwMND. Item D on the CSS-MNDr did not correlate well with item 2 on the ALSFRS-R or the MLS (correlation coefficients of −0.3 and 0.3, respectively). This question focused on saliva problems at night, which could suggest that when lying down saliva is easier to swallow or that use of an NIV machine at night may dry oral secretions to a manageable level. It would be of interest to further investigate the questions with the weakest correlations to the ALSFRS-R saliva question and, perhaps more importantly given the ALSFRS-R question's limitations, the MLS to determine whether there are particular subgroups experiencing problems less common in the wider population of plwMND.

The CSS-MNDr has shown to have good validity and reliability and therefore provides a valuable tool for the assessment of interventions both in trial and clinical care settings. Unlike the other instruments available, the CSS-MNDr considers thick secretions alongside runny saliva and offers a more comprehensive assessment of secretion problems and their impacts on daily life. It is hoped that the CSS-MNDr will facilitate better management of patients with oral secretion problems.

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Declaration of interest

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