# 2023 exceptional surveillance of motor neurone disease (NICE guideline NG42): assessment and management

## Surveillance proposal

We propose to update Recommendation 1.3.1 from:

> 1.3.1 Be aware that people with MND and frontotemporal dementia may lack mental capacity. Care should be provided in line with the Mental Capacity Act 2005' to
>
> *'Be aware that people with MND, **in particular those with concomitant frontotemporal dementia**, may lack mental capacity. Care should be provided in line with the Mental Capacity Act 2005.'*

We will actively monitor the status of ongoing studies:

- the COMMEND trial (COMmitment therapy for people with Motor nEuroN Disease) recruiting approximately 188 people with MND, due to complete in early 2024. The trial compares acceptance and commitment therapy (ACT) plus usual care to usual care alone (Gouldet al. 2022).

- Pondofe et al. (2022), an ongoing systematic review exploring effects of breathing exercises, respiratory muscle training, NIV, manual assisted cough or mechanical insufflation-exsufflation compared to placebo or any combination of the above, standard treatment, or no intervention (recommendation 1.13).

We will not update any other sections of the motor neurone disease (MND) guideline (NG42).

We will not update the guideline on genetic testing, counselling, and sequencing for information and support at diagnosis, or tracheostomy as these topics are out of scope. We will not update the guideline on addition of

mexiletine for muscle cramps, voice, or message banking for communication, arterial or capillary blood gas analysis as part of routine assessment as there is insufficient evidence to warrant the changes.

## *Reason for the exceptional surveillance review*

The Motor Neurone Disease Association, in collaboration with key experts and practitioners, submitted an enquiry to NICE expressing the need of an update of NICE guideline NG42, which was published in 2016. Due to limited available evidence at the time of guideline development, the enquirers suggested revisiting some topic areas where new evidence may now be available, and to also consider new topic areas that are not currently covered in the guideline scope. Topic areas suggested where there may be new evidence are:

- cognitive assessments,
- prognostic indicators,
- organisation of care,
- psychological support,
- cough effectiveness,
- non-invasive ventilation (NIV)

## *Methods*

The exceptional surveillance process consisted of:

- Considering the information and intelligence provided by the enquirers that triggered the exceptional review.
- Literature searches to identify relevant evidence for psychological therapies, and assessment tools to identify cognitive and behavioural changes in people with MND.

- Considering the evidence used to develop NICE guidelines CG105 in 2010 (Motor neurone disease: the use of non-invasive ventilation in the management of motor neurone disease).
- Feedback from topic experts including members of the NICE guideline NG42 guideline committee.
- Examining other related NICE guidance and quality standards.
- Examining the NICE event tracker for relevant ongoing and published events.
- A search for ongoing research from clinicaltrials.gov, European trials registry and the Australian and New Zealand trial registry. Topic areas identified include predictive factors for progression of MND, cough effectiveness, biomarkers of MND/FTD, memantine, and dignity therapy.
- Assessing the new evidence against current recommendations to determine whether to update sections of the guideline.

For further details about the process and the possible update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

### *Search and selection strategy*

The searches retrieved 1175 publications for cognitive and behavioural assessment tools, and 674 publications for psychological interventions for people with MND. The following databases were searched:

- Cochrane Database of Systematic Reviews (CDSR, Wiley): Issue 5 of 12, May 2023
- Cochrane Central Register of Controlled Trials (CENTRAL, Wiley): Issue 5 of 12, May 2023
- MEDLINE (Ovid): 1946 to 24th May 2023

- MEDLINE in-process (Ovid): 1946 to 24th May 2023
- MEDLINE epub ahead of print (Ovid): Ovid MEDLINE (R) Epub ahead of print 24th May 2023
- EMBASE (Ovid): 1974 to 24th May 2023
- PsycINFO (Ovid): 1806 to May week 3 2023

Searches for both topics can be found in **appendix A.**

From the searches, 26 studies were included as new evidence related to the following topics:

- assessment tools to identify cognitive and behavioural changes: we found 14 studies in a search for systematic reviews, randomised controlled trials (RCTs), observational studies, and cross-sectional studies.
- psychological interventions: we found 12 studies for psychological interventions in a search for systematic reviews and RCTs.

We searched for ongoing research through trial registries which identified the following trial:

- cough effectiveness: NCT05819931: Breathing with Amyotrophic Lateral Sclerosis (ALS)

See **appendix A** for details of all evidence considered, and references. Full references are provided at the end of the document.

## *Topic expert feedback*

In this exceptional surveillance review we engaged with topic experts who were recruited to the NICE Centre for Guidelines Expert Advisers Panel to represent their specialty. We received feedback from 5 topic experts (professor in communication, motor speech disorders and augmentative and alternative communication (1), consultant nurse in MND (1), physiotherapist

(1), consultant in palliative medicine (1), and neurologist (1)). We consulted with the topic experts on specific questions for which we needed further advice on regarding cognitive assessments, prognostic indicators, organisation of care, cough effectiveness and non-invasive ventilation (NIV).

## *Information considered in this exceptional surveillance review*

### Cognitive assessments

Recommendation 1.3.1 was made based on consensus of the guideline committee and co-opted expert as no clinical or economic evidence was identified. The committee acknowledged that identification of cognitive change would be of clinical benefit to people with MND and unlikely to be harmful. Identification of cognitive impairments and behavioural change in people with MND at the point of diagnosis could have impact on ensuring that useable and individually tailored equipment is appropriately provided for their needs. Ensuring equipment is tailored can reduce costs to the NHS and improve health outcomes by avoiding provision of inappropriate equipment that eventually has to be replaced. No specific evidence was found for frequency of assessment, however, the committee included cognition and behaviour as an area to be covered at the MDT review in their discussion of the evidence. At the time of development of the guideline, the committee acknowledged that there was no single validated tool specifically to assess people with MND and that a variety of tools were used by psychologists when conducting formal assessments.

The enquirers highlighted that the current wording of recommendation 1.3.1 implies that frontotemporal dementia is the only cause for lack of mental capacity, and that it does not reflect people with MND without dementia could lack mental capacity due to other causes. Additionally, the enquirers highlighted that validated screening assessment tools, such as the Edinburgh Cognitive and Behavioural Screen (ECAS) or the Beaumont Behavioural Index (BBI) have been developed since publication of NICE guideline NG42, that assess behavioural changes in people with MND. The enquirers have suggested that evidence for these assessment tools have differing strengths

in identifying cognitive and behavioural changes and could be more effective at differing points of MND stages.

We assessed the studies suggested by the enquirers which included a relevant systematic review on the validity and diagnostic accuracy of Amyotrophic Lateral Sclerosis (ALS)-specific screening tools (Simon et al. 2019). Other studies suggested by the enquirers did not meet the required study design criteria (Gosselt et al. 2020; Gray et al. 2022; Hodgins et al. 2020; Radakovic et al. 2020). Nguyen et al. 2021 was highlighted by the enquirers and was also identified from the focused search, and is described below.

The focused search of the evidence for cognitive or behavioural assessment identified 14 studies. Simon (2019) and 13 other publications identified were validation studies or diagnostic studies (Aiello et al. 2022; Aiello et al. 2023; Beeldman et al. 2021; Elamin et al. 2017; Greco et al. 2022; Iazzonling et al. 2022; Lule et al. 2014; Niven et al. 2015; Pinto-Grau et al. 2017; Saxon et al. 2020; Tiokrowijoto et al. 2023; Turon-Sans et al. 2016; Wooley et al. 2010). Mostly the population in the studies was people with ALS. The types of assessment tools that were identified in the studies included the Beaumont Behavioural Inventory (BBI), ALS Cognitive Behavioural screen (ALS-CBS), Frontal Assessment Battery (FAB), Edinburgh Cognitive and Behavioural ALS Screen (ECAS), Motor Neuron Disease Behavioural Instrument (MiND-B), Consortium to Establish a Registry for Alzheimer's Disease (CERAD) and Montreal Cognitive Assessment (MoCA) test. These were compared to neuropsychological assessments or another assessment tool as the reference standard. The ALS-CBI, BBI and ECAS were tested among the studies.

Cognitive deficiency with ALS-CBI was detected with a range of 71-86.2% sensitivity and 62-85% specificity compared to neuropsychological and/or neurological assessment as the reference standard in two studies (Turon-Sans et al. 2016; Woolley et al. 2010). Behavioural changes on ALS-BCI had 80% sensitivity and 92% specificity compared to neuropsychological testing (Woolley 2010).

The BBI had a sensitivity of 87.9% and specificity of 78.9% compared to the Frontal Systems Behaviour Scale (FRSBe) at a cut off 7 in detecting mild behavioural changes (n=85) (Elamin et al. 2017). Against the ALS-FTD questionnaire and FAB, BBI had 100% sensitivity and 92% specificity in detecting severe behavioural changes, however, for mild behavioural changes sensitivity and specificity were 50% and 76% respectively (Pinto-Grau et al. 2017).

ECAS had 85% sensitivity and 85% specificity in detecting cognitive impairment compared to neuropsychological assessment (Niven et al. 2015). Saxon et al. (2020) reported the sensitivity and specificity of ECAS in detecting cognitive impairment in people with ALS-FTD (90% and 35% respectively), and in people with ALS behavioural variant frontotemporal dementia (ALS-bvFTD) (78%% and 35% respectively). ECAS had high specificity compared to CERAD (75% to100%) but sensitivity was lower, 33% to 50% (Turan-Sans et al. 2016). Two studies evaluated behavioural impairment or cognitive decline in people with ALS using MiND-B and ACE scores respectively on survival time. In Kaplan-Meier survival analyses the studies showed that deficits in behaviour or cognition were associated with shorter survival time (Nguyen et al. 2021; Xu et al. 2017).

### *Limitations of the evidence*

The population in the studies was ALS, therefore it remains uncertain whether these tools are generalisable to other MND types. Sensitivities and specificities of the different tools reported in the studies vary therefore, it is unclear which tools are appropriate or most accurate for different MND disease stages.

### *Topic expert feedback*

We asked the topic experts if the wording for recommendation 1.3.1 should be amended to make the relationship between MND and frontotemporal dementia clearer. All topic experts agreed with the changes to the wording of the recommendation, however, one topic expert pointed out the importance of conforming to the Mental Health Act, and evidence to show that up to 50% of

people with MND may have cognitive and behavioural change including frontal lobe dysfunction. This may impact on decision making and capacity. Topic expert opinion does not correlate with the committee's consensus about recommendation 1.3.1 however, it is in agreement with the enquirers suggestion to change the wording of the recommendation.

***Impact statement***

Recommendation 1.3.1 was made based on consensus of the guideline committee. The current recommendation wording is: 'Be aware that people with MND and frontotemporal dementia may lack mental capacity. Care should be provided in line with the Mental Capacity Act 2005'

Topic experts were consulted on this query and agreed that the wording should be amended to 'Be aware that people with MND, in particular those with concomitant frontotemporal dementia, may lack mental capacity. Care should be provided in line with the Mental Capacity Act 2005.'

Currently NICE guideline NG42 does not recommend specific assessment tools for cognitive/behavioural assessment. Current recommendation 1.3.2 states that, "if needed, refer the person for a formal assessment in line with the NICE guideline on dementia". In addition to the studies identified by the enquirers, the focused search shows there is new evidence for cognitive/behavioural assessment tools such as the ALS-CBS, BBI, ECAS, FAB and MiND-B. Given the variation of sensitivities and specificities of the tools identified and the populations included in the studies, further evidence is required to determine whether these assessment tools can sufficiently detect cognitive and behavioural changes at different stages of disease progression. As such, there is currently insufficient consistent evidence to change current recommendations. Most new evidence identified are on Amyotrophic lateral sclerosis (ALS) with uncertain generalisability to other MND types.

**Prognostic indicators**

Only one study on an externally validated tool (ALS Prognostic Index) for predicting survival in people with MND was identified during development of the guideline. The study was of low quality due to its observational study

design. While the ALS Prognostic Index was considered a useful tool for predicting survival, the guideline committee thought the tool needed to be validated in a UK cohort of patients who were receiving NHS care before it could be recommended. The guideline committee considered the importance of site of MND onset, age at diagnosis, weight loss, forced vital capacity at diagnosis, and lower ALSFRS or ALSFRS-R scores as predictors of reduced survival.

The enquirers highlighted that the NICE research recommendation on prognostic tools was no longer relevant as research on validating ALS-PI had stalled and new prognostic tools were available that should be considered in the guideline. The studies highlighted by the enquirers were checked for inclusion against the current evidence review protocol. Two studies were identified that were relevant. Caga et al (2016) investigated and established apathy as a critical prognostic factor for shorter survival in people with moderate to severe ALS (hazard ratio 3.8, 95% confidence intervals 1.9 to 7.5, P=0.0001; Cambridge Behavioural Inventory-revised (CBI-R tool); adjusted for cognitive status, disease status and symptom duration at start of study). The second study, Nguyen et al. (2021) showed that the risk of death was 2.53 times higher in people with ALS with behavioural impairment on MiND-B compared to those without behavioural impairment (95% CI 1.3 to 14.6, P=0.003). Behavioural dysfunction using the MiND-B assessment predicted survival and demonstrated that for every unit decrease in the MiND-B, the risk of death increased by 3%. Similar results for cognitive impairment using ACE-R assessment were observed, with shorter survival times in people with cognitive impairment compared to those without (HR 2.0, 95%CI 1.04 to 3.3, P= 0.042), and demonstrated that reduction of 1 unit on ACE was associated with increased risk of death by 4% (Nguyen et al. 2021).

***Limitations of the evidence***

The two studies suggested by the enquirers are relevant to this topic, however, there is potential limitation in selection bias of people recruited from specialised ALS clinics who are more motivated to participate. The use of the CBI-R tool to measure apathy is shown to be a critical factor for survival, it is

unclear whether apathy is commonly measured in practice. There is some evidence for the use of the MiND-B tool in people with ALS, however, it is unclear whether this tool could be generalisable to other MND types.

***Topic expert feedback***

Three topic experts identified ECAS, and one topic expert identified MiND B as useful assessment tools to identify cognitive and behavioural changes. Three topic experts agreed that apathy could also be a prognostic indicator but not always being identified and the CBI-R is not used in practice. One topic expert highlighted that apathy could be linked to social cognitive issues in a small group of people with MND and linked to people with depression (although the prevalence is lower than what might be expected). Topic expert opinions correlated with the evidence identified, specifically for the use of the MiND-B assessment tool to predict survival. The topic experts were in agreement as to the merits of apathy as a prognostic indicator, however, there is uncertainty for the use of the CBI-R assessment tool in practice.

***Impact statement***

The current NICE guideline NG42 does not make recommendations on the use of specific cognitive/behavioural and prognostic tools. There is insufficient new evidence to update the existing recommendations to be specific about which tools to use. The new evidence identified on cognitive and behavioural assessments for prognostic indicators is for ALS with small participant numbers and is uncertain in generalisability to other MND types.

**Organisation of care**

During development of the guideline, the committee acknowledged that access to health professionals outside of the core MDT was important and could be involved in more targeted care. The evidence identified in the review was based on 8 studies (one RCT, one before and after study, and 6 cohort studies). Most studies compared multidisciplinary care to general neurological care. One study compared multidisciplinary care plus coordinator care to multidisciplinary care alone. Two studies included a psychologist in the core MDT. The evidence was limited because of outcomes being rated as very low

quality and the composition of the MDT being varied among the studies. However, there was a clinical benefit of the involvement of a MDT in a community or hospital-based setting on survival time and hospital stay. There was no clinical benefit of having an independent, additional coordinator to an MDT. The committee did not wish to specify who should coordinate care for the person with MND as this may differ for different geographical locations.

The economic model evaluated the trade-off between benefit observed in the clinical evidence and additional costs associated with MDT care such as additional staff time, increased NIV use and Riluzole plus additional costs of general MND care associated with increased survival. The committee discussed the assumptions made in the economic model: 1. cost of MDT care was simply added on to the average costs associated with treating an individual with MND (i.e., usual care costs); 2. the model assumed no cost savings generated from MDT care; 3. the model assumed no quality of life improvement for people with the MDT arm. Quality of life may be underestimated by the EuroQol-5 dimension (EQ-5D) because the model assumes no quality of life improvement for people in the MDT arm. Thus, any intervention that extends life in an MDT cohort is unlikely to be cost-effective even if it only costs a small amount. The committee agreed that cognition and behaviour was important to assess, manage and review regularly.

The MDT composition in the health economic model was the same as that identified in the clinical studies. The cost of MDT was calculated by the committee using expert consensus. The health economic model for MDT configuration was not shown to be cost-effective at £20,000 per QALY threshold in the base case, and it was acknowledged that the model undervalued quality of life of individuals with MND. The model was sensitive to small increments in quality of life, any psychological improvement brought by clinical psychologist in an MDT could potentially bring the incremental cost-effectiveness ratio (ICER) within NICE's acceptable quality- adjusted life year (QALY) threshold.

In the committee discussion within the guideline, it was acknowledged that a multidisciplinary team (MDT) with the core members currently recommended

would be beneficial for patients, although there were uncertainties in the health economic model. Any changes or addition of more core members would require good quality new evidence to allow re-analysis of the health economic model. Current recommendations on the core members are not exhaustive or exclusive and recommendation 1.5.5 does allow prompt access to clinical psychology and neuropsychology. There is no new evidence that specifically evaluates the effectiveness of a MDT with psychologist as a core member.

The enquirers challenged the absence of a clinical psychologist in the core multidisciplinary team (MDT) (recommendation 1.5.4) because they believe new evidence suggests psychological wellbeing is a key factor for improving quality of life in people with MND.

Studies suggested by the enquirers did not meet the inclusion criteria of both the review protocols for this topic. Ando et al (2022) and Zarotti et al (2019) were both qualitative studies, and Young et al (2019) was not a comparative study.

***Limitations of the evidence***

No new studies have been identified in this topic area therefore, it is unclear if the addition of a psychologist in the MDT is clinically or cost-effective.

***Topic expert feedback***

We asked the topic experts whether a psychologist was part of the core MDT in clinical practice. Two agreed that a psychologist was key to MDT working, however, 3 experts did not agree because there is a lack of psychologists in the NHS and access to psychological services on a regular basis is currently challenging in the system. One expert said that ideally psychologist involvement in the MDT would be beneficial, but in practice this was not the case. Only one expert was aware of any studies looking at effectiveness of MDT organisation that included a psychologist.

***Impact statement***

Recommendations were based on consensus of the guideline committee. Due to a lack of new evidence, implementation challenges of having psychologist input routinely in the MDT and the link already established to psychological support in Recommendation 1.5.5, there is no impact on the current recommendations on organisation of care.

**Psychological support**

Recommendations 1.6.1 to 1.6.6 were based on qualitative evidence highlighting important areas included coping with diagnosis, understanding the disease, acceptance, coping with a changed life, change in relationship, carers, sources of support, and decision making. The committee were aware of the importance of psychological and emotional issues for all other areas of disease management, noting that acceptance of the disease helped people to cope with all aspects of symptom management. The committee recognised that healthcare professionals who deliver psychological support must adapt the content and delivery of this support to the needs of the person with MND. Everyone has different requirements for support, and therefore the interactions must be led by the person. The committee distinguished information emotional support and counselling from formal psychological support in the recommendations. Many people with MND and their families can be helped with informal support, including involvement with support groups and charities such as those associated with the MND Association. The most appropriate psychological intervention(s) will depend on the nature and severity of the individual's problems, any history of previous psychological problems and the quality of social support available. A range of psychological interventions can be offered by both the statutory and voluntary sectors. Health and social care professionals offering day-to-day care provide much general psychological support to patients and carers. They play a key role in psychological assessment, and in the prevention and amelioration of distress.

The committee highlighted that practitioners should be alert to the requirement for formal psychological assessment and support and the need to refer to psychological and neuropsychological services. They highlighted the need for

appropriate treatment for people with MND who are also suffering from depression. They felt that the issue is covered by CG91 NICE guideline.

The enquirers highlighted the absence of recommendations on specific psychological therapies that may be clinically and cost-effective to improve quality of life and psychological wellbeing in people with MND

Two studies were suggested by the enquirers. One study had a cross-sectional study design and did not meet the inclusion criteria of the guideline review protocol (Lapin et al. 2022). The second study was a qualitative study that explored needs and preferences for psychological interventions of people with motor neuron disease (Weeks et al. 2019). No study on clinical effectiveness of psychological support was provided by the enquirers.

Several studies on clinical and cost-effectiveness of psychological interventions for people with MND and their carers were identified from the focused search of this surveillance review.

One RCT (N=15) compared 16 weeks of CBT (stress coping model) in psychologically distressed patients with ALS and their caregivers to usual care alone (Groenestijn et al 2015). CBT consisted of 5 to 10 sessions (individual or group) provided by three trained and instructed psychologists using behavioural and rational-emotive principles in addition to usual care. Outcome measures included the Mental Component Summary (MCS) of the SF-36 scale, ALSAQ-40-EF, Hospital Anxiety and Depression Scale (HADS) and Caregiver Strain Index (CSI). The MCS of the SF-36 score assessed in caregivers improved in the CBT group compared to usual care. Similarly, ASLAQ-40-EF in people with ALS improved in the CBT group compared to usual care. No significant differences between the CBT group and usual care group were found in psychological distress (Hospital Anxiety and Depression Scale) (p =0.26).

One RCT (N=74 people with ALS and progressive muscular atrophy (PMA) and their caregivers compared a support programme delivered by a psychologist based on Acceptance and Commitment Therapy (ACT) for 12 weeks to a control group (De Wit et al 2020). No significant differences were

observed on psychological distress or quality of life, however, improvements in self-efficacy were observed in the intervention group including caregivers. Nearly 50% of participants did not complete the intervention which may have contributed to lack of efficacy observed in outcomes.

One RCT (N=100) compared an 8-week ALS-specific mindfulness-based stress reduction programme to usual care was identified (Paganini et al 2017). Significant differences between MBSR and usual care groups were observed in measures for quality of life, anxiety, depression, negative emotions and interaction with people and the environment.

Another RCT (N=48) compared an expressive disclosure intervention with a control group in people with ALS (Averill et al 2013). The patients in the intervention group showed better wellbeing status than the control group at 12 weeks after the intervention, but not at 26 weeks. Expressive disclosure therapy was only effective in those with low emotional expression which suggests that the intervention may not be affective in later stages of ALS.

One RCT (N=30) compared 12 sessions of active music therapy plus standard care to standard care alone in people with ALS (Raglio et al 2016). Quality of life improved on the McGill Quality of Life Questionnaire global scores in the active music therapy group compared to standard care alone (P <0.035).

***Limitations of the evidence***

The trials identified include small numbers of people with ALS. The types of psychological interventions are different from each other therefore difficult to compare. The impact of these interventions on health outcomes is unclear in general, and it is uncertain about the generalisability to other MND types.

***Topic expert feedback***

No topic expert feedback was elicited on this area.

***Impact statement***

The current guideline does not include recommendations on specific psychological interventions for people with MND. There is currently insufficient evidence to support the inclusion of this topic area in the guideline. The evidence identified on this topic includes people with ALS and generalisability to other MND types is unclear. Inclusion of this topic could impact on other areas of the guideline including organisation of care, cognitive assessment tools, and prognostic indicators.

**Cough effectiveness**

Recommendations 1.13.1 to 1.13.4 were developed based on the committee's experience. The committee highlighted that the evidence did not support one cough augmentation technique over another. In current practice, regular breath stacking was used for ineffective cough, however, there was no evidence to compare unassisted versus assisted breath stacking. There was no clear clinical difference between breath stacking and other cough augmentation devices. The committee agreed that doing cough augmentation was better than doing nothing, therefore their informal consensus was used to make recommendation for cough augmentation techniques first and are associated with reduced staff time and cost. Breath stacking (manual followed by assisted) and then mechanical cough assisting techniques should be considered when cough augmentation techniques are ineffective or inappropriate.

The enquirers highlighted more recent evidence on cough effectiveness interventions specifically peak cough augmentation. The evidence they suggested was based on efficacy of cough augmentation, through a combination of interventions rather than any one intervention in isolation. They also highlighted the importance of acknowledging the impact of cognitive and behavioural changes on people's acceptability of cough augmentation and their ability to carry out the intervention. The enquirers pointed out that people's cognitive and behavioural states need to be considered prior to carrying out cough augmentation. Cognitive and behavioural impact on cough

augmentation was not discussed by the guideline committee during the development of recommendations on this topic area.

Studies suggested by the enquirers were checked for relevance. One RCT of 30 people with ALS by Nicolini et al (2022) did meet the inclusion criteria in the review protocol. Cough assist plus expiratory flow accelerator was compared to cough mechanical assisting. Outcomes included changes in respiratory function tests, gas exchanges, and peak cough expiratory flow. Improvement in respiratory function tests was reported in both groups but more so in the cough assist plus expiratory flow accelerator group. No differences in gas exchange between both groups was observed. Both groups reported similar increases in perceived cough efficacy and no adverse events were identified.

A further search of evidence identified limited data from one small, low quality RCT that reported improvements in respiratory function and peak cough expiratory flow when cough assist and expiratory flow accelerator devices were performed in combination compared to cough assist alone. No studies were identified regarding the impact of patient's cognitive and behavioural changes on how cough augmentation should be delivered.

***Limitations of the evidence***

There is insufficient new evidence on this topic area with only one small study identified.

***Topic expert feedback***

We asked the topic experts if they were aware of any studies on effectiveness of cough augmentation through combined or single interventions for people with MND and reduced ability to cough. None of the experts identified any studies in this topic area.

Additionally, topic experts were asked whether mechanical insufflation-exsufflation (MI/E) plus expiratory flow accelerator (EFA) are routinely used together in practice in people with MND. While 4 topic experts agreed that this MI/E and EFA were routinely given in practice, one expert stated that it would

depend on the indication for combined treatment, and patient's peak cough flow (PCF) and if the threshold level for secretion clearance can be achieved with a single intervention.

Topic experts were asked whether changes in cognition and behaviour were associated with changes in cough efficacy. Four of the experts agreed that cognitive and behavioural changes were associated with changes in cough efficacy. One expert commented that coordination of breath and following instructions may become more challenging and depended on the individual. One expert did not know of any studies on this topic. Only 2 topic experts agreed on an established association between ineffective cough due to secretion encumbrance, morbidity, and mortality.

***Impact statement***

There is no impact on current recommendations regarding cough effectiveness. Current recommendations are permissive of multiple interventions to improve cough effectiveness and evidence was insufficient to allow for formulation of more specific recommendations on the association between cognitive/behavioural status and cough efficacy.

**Non-invasive Ventilation (NIV)**

Enquirers suggested that a medical history check should be included as part of the discussion about NIV in recommendation 1.14.2. The evidence underpinning this recommendation was qualitative and did not include themes related to medical history checks. The committee did not discuss this issue when developing the recommendation. However, this suggestion is more relevant to recommendation 1.14.7 because recommendation 1.14.2 is relating to information and support. The evidence underpinning recommendation 1.14.7 was very limited and of low quality. The committee used the EFNS task force guideline (Anderson 2005) and the Motor Neurone Disease Association review (www. Mndassociation.org) on the management of respiratory insufficiency in patients with MND/ALS for discussion. Based on their knowledge, experience and expertise, the committee proposed a list of

symptoms and signs for routine monitoring to detect potential respiratory impairment through committee informal consensus.

The enquirers also challenged that arterial or capillary blood gas assessments should be carried out as part of routine assessment of respiratory impairment rather than based on $SpO_2$ assessments as currently recommended in 1.14.11. This recommendation was based on the committee's expertise and knowledge due to absence of clear evidence about which respiratory function tests were best to detect respiratory impairment. The committee agreed to recommending SpO2 as a first-line routine initial screening because it was practical to use, less stressful for patients, and could be carried out by most health professionals. A cut-off of less than 90% was used as the reference standard in the limited evidence for nocturnal SpO2 (one cohort study), however, the committee felt that the cut off for daytime SpO2 for people with MND should be higher in order to detect respiratory impairments appropriately and early. Based on the committee's consensus, further arterial or capillary blood gas analysis was recommended if SpO2 was less than 92% (in people with known lung disease) or if SpO2 was less than 94% (in people with no lung disease).

The enquirers further challenged that the current wording of recommendations 1.14.10 and 1.14.17 'symptoms and signs' (instead of 'symptoms and/or signs') sets a high trigger threshold for further respiratory impairment assessments or respiratory function tests respectively and increases the likelihood that people with MND requiring further assessment are excluded from referral by practitioners. Both recommendations 1.14.10 and 1.14.17 were based on consensus and expertise of the guideline committee. During discussion of the evidence, the committee did not discuss the wording or threshold for assessment of respiratory impairment or respiratory function was identified.

The enquirers did not highlight any new evidence to support their queries about recommendations 1.14.7, 1.14.10, 1.14.11, and 1.14.17. For recommendation 1.14.2, neither the evidence included in the guideline, nor the committee discussion included any information about checking medical

history as part of discussion about NIV. In addition, recommendation 1.14.2 refers to information and support therefore, the suggestion by the enquirers to check medical history may be more appropriate as part of identification and assessment of respiratory impairment (recommendation 1.14.7). A further search of the evidence did not identify any relevant new studies on this topic area.

No new evidence was identified that suggests arterial or capillary blood gas tests should be used instead of SpO2 (recommendation 1.14.11). Similarly, no new evidence was identified to support the change of wording of 'symptoms and signs' to 'symptoms or signs' in recommendations 1.14.10 and 1.14.17.

***Limitations of the evidence***

No new evidence was identified in this topic area.

***Topic expert feedback***

Regarding recommendation 1.14.11, topic experts were asked whether arterial or capillary blood gas analyses should be conducted as part of routine assessments rather than based on reduced $SpO_2$ measurements. Two topic experts agreed that arterial or capillary blood gas analyses should be conducted routinely because $CO_2$ measurements can be obtained that are more sensitive. Three topic experts disagreed because blood gases may not be easily available (e.g., outpatient clinics or domiciliary care) due to costs, and are more invasive than $SpO_2$.

We asked the topic experts about the wording in recommendations 1.14.10 and 1.14.17 in which 'symptoms *and* signs' was used. The enquirers highlighted that the current wording set a high trigger threshold for further assessment. Two topic experts agreed with the change to the wording proposed by the enquirers whereas 3 topic experts disagreed that the wording should be changed or set a lower threshold for further assessment. One topic expert suggested that the wording could be changed to 'symptoms and/or signs' to include both.

We asked the topic experts of any issues for specific subgroups within the MND population. They were not aware of any, except people living in areas where a local MND MDT is not available and that guidelines are not being used in all areas effectively therefore, not all people with MND are receiving standard care recommended by the guideline.

Topic experts agreed that medical history should be checked when discussing NIV, and that medical history was checked as part of routine practice.

***Impact statement***

There is no evidence to support a change to the wording of recommendation 1.14.2, or changes to wording relative to 'symptoms and signs' in recommendations 1.14.10 and 1.14.17. There is no new evidence to support the routine use of arterial or capillary blood gas analysis in recommendation 1.14.11. There is no new evidence on whether a higher or lower threshold is appropriate for symptoms and signs to perform respiratory function tests for respiratory impairment or the circumstances in which NIV should be offered. Although topic experts agreed that medical history should be checked, there is no new evidence to support a recommendation for this topic.

## *Other relevant NICE guidance*

We checked for NICE and other guidelines that may be relevant for people with MND.

NICE guidelines:

- NICE NG222: depression in adults: treatment and management
- CG123: common mental health problems: identification and pathways to care
- CG136: service user experience in mental health: improving the experience of care for people using adult NHS mental health services.
- NG142: end of life care for adults: service delivery

## *Equalities*

NICE conducted an equalities impact assessment during the development of the guideline which outlined statements regarding access to care and equipment to meet the individual needs of a person. Based on feedback from topic experts, one expert identified an issue of access to services for people living in areas where there is no local MND MDT. It was highlighted that the guidelines were not being used in all areas effectively and therefore action was needed to ensure that all people with MND receive the standard of care recommended in the guidelines.

See **appendix B** for the equalities and health inequalities assessment.

## *Overall proposal*

The enquiry that triggered this review highlighted relevant challenges to elements of care for people with MND. Very limited evidence was identified to support updating the guideline at this time in any of the areas raised by the enquiry.

For further details and a summary of all evidence identified in surveillance, see **appendix A.**

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