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Delivering Effective Non-Invasive Ventilation in Motor Neuron Disease

Submission date 21/03/2025	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 16/04/2025	**Overall study status** Ongoing	
Last Edited 16/04/2025	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims

Motor neuron disease (MND) affects 1 in 300 people. There is no known cure. Most people die due to weakness of the muscles that control breathing. Non-invasive ventilation (NIV) is the only treatment shown to help people with MND live longer, feel better and enjoy life more. NIV involves wearing a mask over the face to support breathing and many people find it hard to use. More than half of people are not getting the full benefits, either because they are unable to use it for long enough or because it does not work well.

All patients should receive good quality NIV support, no matter where they live or which hospital they go to. This support should use current and new technologies in a way that's affordable and sustainable. Right now, the best ways to provide NIV support aren't being used everywhere, and very few hospitals are using telemonitoring for NIV, which would negate the need for patients to travel to hospital. Our earlier research found this is because healthcare professionals and hospitals aren't always clear on what to do, don't always involve everyone needed, don't always take the right actions, and don't always check how well patients are doing.

To make NIV support work better, both individual healthcare workers and entire hospital departments need to change how they work. We've used well-known ideas (theories such as 'Normalisation Process Theory', and frameworks such as the 'Consolidated Framework for Implementation Research') about how to improve healthcare to create a plan (which we have called our DENIM 'programme theory'). We think this plan will help healthcare teams provide better NIV support for people with motor neuron disease (MND). We need to test this plan against the current standard of care, to understand if it does deliver better NIV support.

The ‘plan’ (also called an implementation strategy) aims to deliver patients a more intensive /supportive package of care when setting up non-invasive ventilation (NIV) (including using telemonitoring). The DENIM Trial wants to know whether this increases the amount of time people with motor neuron disease (MND) spend using their NIV? Do more people manage four or more hours every day compared to usual care?

Who can participate?

People who are 18 years or over, with a diagnosis of MND confirmed by a consultant neurologist and with a clinical diagnosis of respiratory insufficiency according to local protocols, published guidelines and/or specialist opinion. Patients must have respiratory insufficiency judged by the treating clinician to be severe enough to warrant long term domiciliary NIV and requiring NIV

optimisation within the duration of the study (12 weeks). Patients may start their NIV at home, in an outpatient setting or in hospital if hospital stay is less than or equal to 3 days post NIV initiation. Pateints should be able to provide informed consent. Adults will also be eligible if they are agreeing to try NIV and able to provide assent (evidence of agreement to take part in the study) but unable to provide informed consent will be able to participate if a consultee (close relative, informal carer, immediate care team) provides a consultee declaration.

What does the study involve?
In summary:
Two visits (at the setup of the patients NIV machine for trial consent and some initial questionnaires about their breathing) and at 12 weeks after starting NIV where they are asked the same questionnaires about their breathing. The patient will not need to attend any additional hospital appointments. For some participants, they may receive extra support from their care team, during the 12 weeks.
In detail:
A member of the patient's care team at individual NHS Trusts will identify potential participants and post them a letter and information sheet about the study (including summary in the appropriate language). The letter will be sent in advance of their NIV initiation clinic appointment. Where inpatient recruitment is occurring, a letter and information sheet will be given in person and the patient and family given sufficient time to read, ask questions and consider the study. During the patient's clinic appointment they will be given the opportunity to ask questions from both the clinical and research team. NHS language interpretation services will be used where required.
Participants can provide written consent. Witnessed consent can be provided for patients unable to speak, read and/or write and can include the use of a communication aid. Participants may choose to nominate a consultee for the duration of their involvement in the trial. For participants unable to consent due to cognitive decline, a consultee declaration may be sought.
The patients care team will set up the NIV machine, so it uses the mobile internet to send information to the care team and the research team. They will also ask the patient to complete some questionnaires about their breathing symptoms and quality of life.
For patients whose hospital is in the 'control arm' (not yet trained in the new way to delivering support), they will receive the normal amount of support that their care team provides for the next 12 weeks.
For patients in hospitals who have received the new training/'plan', they may have more frequent contact with their care team. Once using NIV at home, the patients care team will use telemonitoring to check the ventilator data frequently during the first 12 weeks. This means the care team will contact the patient at set times (at least four times in the first two weeks, then at least four further times, in the next 12 weeks after starting NIV), and whenever they notice any issues that need adjusting. They will find out the best way to contact the patient, which might include telephone, text, email or video. They can also contact a carer if preferred. The care team can provide advice and support and make changes to your ventilator settings remotely. They will also explain how to contact them if there are any concerns.
For the study, the research team will access pseudonymous data (this is where data will be given a code, instead of using a name) from your NIV machine to measure how many hours per day the machine is used and how it is working.
The researchers will also ask you to complete some more questionnaires about your breathing symptoms and quality of life at 12 weeks. These can be completed at home via post, telephone or online. Patients will also be asked to wear an oxygen monitor on their finger whilst asleep at home for one night which will be delivered in the post and collected from them.
Participants will not need to make extra visits to the hospital.

What are the possible benefits and risks of participating?
There are no guaranteed benefits to participating in this research. The extra monitoring and support from care teams may help patients to adjust to and use NIV. However, we don't know this for certain, which is why we are doing this study. By taking part, patients will be helping us determine the best way to support people with MND to use NIV effectively. This will inform the treatment of future patients.
The main difference with the new approach is that patients will have more contact with their care team during the first 12 weeks of starting NIV. This is unlikely to be a burden as patients tell us they value regular contact, advice and support from their care team when starting NIV. There are no expected additional risks from taking part.

Where is the study run from?
The project is being carried out by a team of researchers from the Sheffield Centre for Health and Related Research (SCHARR) at The University of Sheffield and Sheffield Teaching Hospital NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
September 2024 to January 2028

Who is funding the study?
This study is funded by the National Institute for Health Research Health and Social Care Delivery Research (UK), reference NIHR158715.

Who is the main contact?
The main contact for the study is the Denim Trial Manager – denimtrial@sheffield.ac.uk

Study website
https://www.denim-mnd.co.uk

Contact information

Type(s)
Public, Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
334849

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 58757, NIHR158715

Study information

Scientific Title
Delivering an implementation intervention to healthcare professionals, aimed at providing an intensive/supportive package of care when setting up non-invasive ventilation (including using telemonitoring), for people with motor neuron disease

Acronym
DENIM

Study objectives
The addition of a highly intensive, theory-informed, goal-based NIV optimisation package during the first 12 weeks of NIV initiation will lead to increased NIV adherence (defined as the number of days in which patients use NIV for >4hr/day during week 9-12) compared to usual care NIV initiation practices in patients with motor neuron disease.

Objectives:
1. To conduct a stepped wedge cluster randomised controlled trial to detect if the addition of highly intensive, theory-informed goal-based approach during the first 12 weeks of NIV initiation increases NIV use and effectiveness;
2. To conduct a process evaluation showing how healthcare professionals' self-reported

normalisation of this new approach to NIV optimisation within clinical teams is associated with wear time and other measures of success, with pathways to outcome further elaborated through observations, interviews and surveys;
3. To conduct a Cost-Effectiveness evaluation alongside a clinical trial and long-term cost effectiveness modelling, from an NHS perspective.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 25/02/2025, Leeds East REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8357; leedseast.rec@hra.nhs.uk), ref: 25/YH/0019

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See outputs table

Health condition(s) or problem(s) studied
Non-invasive ventilation in motor neuron disease

Interventions
The DENIM Trial is an implementation hybrid trial, testing a theory-based implementation strategy aimed at improving the delivery of non-invasive ventilation (NIV) to people with motor neuron disease (MND).

DENIM will be a multicentre study involving respiratory teams from different hospitals who are involved in the setup of NIV for people with MND. As well as testing the effectiveness of the theory-based intervention—a new intensive NIV initiation service (telemonitoring, education package, additional patient support, etc.)—DENIM is interested in understanding the process of implementation and how to better include people from underrepresented backgrounds in MND research.

The main trial is a stepped-wedge, cluster randomisation controlled trial design. In practice, this means that 12 hospitals will join the study and all hospitals will recruit people with MND (who require NIV to be set up) to the control arm. The control arm participants will receive the usual care that their hospital provides for NIV setup and support.

Hospitals will be put in groups of two (clusters). Every three months, a cluster (group of two hospitals) will be randomly assigned to switch to the intervention arm. The intervention arm will involve the healthcare professionals receiving a training package and other implementation elements such as identifying 'champions', attending educational meetings, identifying barriers and strategies specific to their hospital through surveys and observations. Hospitals will also be provided with telemonitoring capabilities and training. From this point onwards, all participants recruited by the hospital will be considered in the intervention arm, because these patients will receive a more intensive level of support from their respiratory team.

Hospitals that remain in the control arm will continue to recruit participants to the control arm until they are randomly allocated to switch to the intervention arm.

The reason for the cluster-stepped wedge design is that it is impossible to have patients in the same hospital in both arms of the study at the same time. Based on experience in our pilot study, we believe once staff are trained to deliver the intervention, there will be crossover because they will deliver components of that intervention to all patients, regardless of allocation. We cannot randomise at the hospital level because of the variation in hospital practice and cannot randomise at the staff level as the staff teams share caseloads. We cannot run a waiting-list trial as it would be unethical to delay NIV optimisation.

Our hypothesis is that more participants in the intervention arm will reach greater than four hours a day use of NIV when compared to the control arm. We also hypothesise participants in the intervention arm will have more effective ventilation (defined by their levels of oxygen saturation measured overnight), better quality of life, and longer survival.

Research Timelines

The study will begin recruiting control arm participants in May 2025. All sites will open between May-October 2025. The first site will switch to the intervention arm in October 2025, with a cluster switching every three months thereafter, for 24 months (96 weeks). The study (data collection) runs for 27 months (108 weeks). Participants give data actively for 12 weeks from NIV initiation. Survival for all participants will be collected at month 27 (week 108).

Recruitment Processes

A screening log will be maintained for each site to document all potential participants screened, whether they were recruited, and any reasons for non-recruitment where this information is available.

A member of the patient’s care team will identify eligible participants that have been referred to a site for NIV. A letter and information sheet (including a summary in the appropriate language) will be provided by their care team in advance of their NIV initiation clinic appointment. A member of their care team will approach the potential participant at their NIV initiation visit. During their clinic appointment, they will be rescreened to check eligibility and given the opportunity to ask questions from both the clinical and local research team. No study-related procedures will occur before the approved consent form is completed, other than initial case note review for eligibility. We will use NHS language translation or interpretation services where required. If the participant wishes to take part, they will complete the written consent form. People with MND may have a range of disabilities including difficulty speaking and/or writing. Witnessed consent can be provided for patients unable to speak, read, and/or write and can include the use of a communication aid. Participants will be asked to nominate a consultee for the duration of their involvement in the trial. The consultee will be consulted if the patient

participant loses capacity during their active participation in the trial (12 weeks). Participants without capacity at consent may be recruited with personal consultee consent.

Patients whose NIV is initiated in emergency or inpatient settings can be approached and consented within 72 hours of NIV initiation and before discharge. Whilst it is recommended that patients are consented on the day of the NIV initiation, if this is not possible, they can be provided with the telemonitoring equipment as part of the usual care. Consent and any baseline data collection can then be completed remotely. Where inpatient recruitment is occurring, a letter and information sheet will be given in person and the potential participant given sufficient time to read, ask questions, and consider the study.
Patients will also receive a copy of the PIS and their consent form to keep. Original copies will be kept in the investigator site file and made available to CTRU. Where 'easy read' documents are shared, participants will also be provided with the PIS.

If a participant declines to take part, they may be invited to take part in an interview study to understand their reasons for declining and how MND research can be more inclusive. A consent to contact form will be completed in this instance to allow the central research team to collect and store their data for the duration of the trial.

All participants will complete baseline questionnaires at their NIV initiation/consent appointment. All participants will receive a ventilation device from their usual hospital stock; these will have telemonitoring capabilities. However, control arm participants will receive the usual amount of support and telemonitoring their hospital provides, and this may mean they do not have their telemonitoring capabilities activated (as per sites' usual care).

Ventilators will collect data on usage and effectiveness automatically and will either store data on the device or transfer that data to the site via a modem/cloud-based system.

Baseline: Questionnaire completed in person at NIV initiation visit.
Week 4: Data collected automatically by ventilator.
Week 8: Data collected automatically by ventilator.
Week 12: Participant questionnaires completed. Collected by postal, online, or telephone (depending on participants' needs).
Survival: Medical record data on survival at month 27.
Participants (with support from carers) in the intervention arm will receive additional NIV support on the telephone at weeks 2, 5, 10 days, 2, 3, 4, 8, 12 weeks post initiation + ad hoc (e.g., following patient contact). Staff can remotely adjust NIV settings (either using the device or by telephone), provide different masks, and communicate and provide support to patients/carers as needed.

Process Evaluation

A process evaluation is integral to the design of the study. The process evaluation is embedded throughout the trial. It will explore in detail how well the intervention (the implementation package, including training for healthcare workers and a worksheet for contacts with participants) works in real healthcare settings, whether it is acceptable for staff and patients, and what barriers and facilitators there are. A multiple case design will be used, conducted at all 12 sites.

Ethnographic Observations

Participants in the intervention arm will have optional consent to ethnographic observations (recorded on the main trial consent form). A member of the central research team, with local Trust permissions, will observe participant-healthcare professional interactions during NIV support sessions.

NOMAD Survey

At the beginning, during (6 months after switching to the intervention arm), and at the end of the study, all site staff will be invited to complete the NOMAD questionnaire.

Patient and Carer Interviews

Participants in the intervention arm will be purposively sampled and invited to take part in one interview to understand their experience of the support they have received. Per site, one to two participants will be recruited, alongside a family member or carer. Written informed consent (in line with the main study processes documented in the study-specific SOP) will be taken at the interview, adapted to the participants' needs. Patients and carers can choose to be interviewed together or separately.

Site Staff Interviews

Site staff (healthcare professionals involved in the care of participants on NIV) will be invited to be interviewed (two per site). Written informed consent will be obtained at the start of the interview. The interview will be conducted face-to-face or by video call.

ACCESS Sub-study: Understanding Inclusion in MND Research

Patients who declined to participate in the main trial will be given optional consent to be contacted by the research team to further understand their reasons for declining. Informed consent will be taken prior to the interview using the study consent processes outlined above. The interviewer will establish the most accessible way to conduct the interview, and translation /interpretation services will be used as appropriate.

Intervention Type
Device

Pharmaceutical study type(s)
Not Applicable

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
NIV

Primary outcome measure
NIV usage (the number of days in which patients use NIV for >4hr/day during week 9-12), measured automatically by the ventilator machine.:
1.1. NIV usage: NIV usage from ventilator machine (first 14 days, first 28 days)
1.2. Calculation of the number of days in which patients use NIV for >4hr/day

Secondary outcome measures
1. NIV usage (first 14 days, first 28 days, weeks 9-12) measured by the ventilator machine
1.1. The average (mean) daily usage
1.2. The number of patients achieving >4hr/day for >70% of nights
2. Nocturnal respiratory insufficiency, measured by overnight oximetry, for a single night at week 12
3. Time spent with oxygen saturations <90%, measured by overnight oximetry, for a single night at week 12
4. Time spent in oxygen desaturation index (ODI) of 4%, measured by overnight oximetry, for a single night at week 12
5. Patient reported outcome measures: collected at baseline and week 12
5.1. Quality of life (McGill quality of life questionnaire, developed for patients with a life-limiting illness)
5.2. Dyspnoea-12 (measuring respiratory symptoms, sensitive to change)
5.3. S3NIV (measures respiratory symptoms, sleep quality, and NIV-related side effects)
6. Health and social care resource use questionnaire, including EQ5D, collected from participant at week 12
7. Survival, collected from medical records, follow-up minimum 12 weeks, maximum of 27 months (week 108)

Exploratory outcomes
8. Ventilator effectiveness, collected from data report from ventilator for the first 14 days, first 28 days, and weeks 9-12
8.1. Tidal volumes
8.2. Ventilator asynchronies
8.3. Apnoea hypopnoea index
8.4. Leak
9. Nocturnal evidence of REM-related desaturation through overnight oximetry, Week 12
9.1. Evidence of REM-related desaturation trace

Explanatory implementation outcomes
10. Assessment of changes in barriers and facilitators to implementation at site level, pre and post intervention (NOMAD survey given to healthcare professionals during the site control arm, week 4 after intervention switch and end of the trial)
11. Fidelity: Percentage completeness of the first consultant workbook (intervention arm), assessed throughout site intervention arm
12. Fidelity: Number of times remote monitoring was reviewed at the pre-specific times, assessed throughout site intervention arm
13. Fidelity: Number of times workbook was reviewed per participant, assessed throughout site intervention arm

Overall study start date
01/09/2024

Completion date
31/01/2028

Eligibility

Key inclusion criteria

Trial participant inclusion criteria:
1. Patients aged 18 years or over.
2. Have a diagnosis of MND confirmed by a consultant neurologist
3. with a clinical diagnosis of respiratory insufficiency according to local protocols, published guidelines and/or specialist opinion.
4. Respiratory insufficiency judged by the treating clinician to be severe enough to warrant long term domiciliary NIV and requiring NIV optimisation within the duration of the study (12 weeks).
5. NIV initiated at home, in an outpatient setting or in hospital if hospital stay is less than or equal to 3 days post NIV initiation.
6. Able to provide informed consent. Adults agreeing to try NIV and able to provide assent (evidence of agreement to take part in the study) but unable to provide informed consent will be able to participate if a consultee (close relative, informal carer, immediate care team) provides a consultee declaration.

Process evaluation patient interviews inclusion criteria:
1. Have consented to participate in DENIM
2. Are in the intervention arm
3. Are able and willing to participate in interviews (various options for facilitation available) and /or ethnographic observations
4. If relevant, are willing to share their preferred language for participation with the research team, to allow an appropriate researcher to be identified.

Process evaluation family/carer inclusion criteria:
5. Relative/friend has consented to participate in DENIM
6. Are able and willing to participate in interviews and/or ethnographic observations

Process evaluation staff interview inclusion criteria:
7. Direct contact with at least one patient who is participating in DENIM
8. Are able and willing to participate in interviews and/or ethnographic observations

ACCESS sub study inclusion criteria:
1. From an ethnic minority and/or where the patient's main language is not English
2. Or with low levels of digital health literacy (either those identified by the site teams or those scoring < 7 on the 3-Item Measure of Digital Health Care Literacy at baseline)
3. Or women over 80 years with bulbar onset disease

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 252; UK Sample Size: 252

Key exclusion criteria
1. Already initiated on NIV/CPAP for MND or another reason
2. Using tracheostomy ventilation
3. No way to connect the ventilation software to the internet whilst in the community
4. Patients not requiring optimisation within 12 weeks (e.g. those given the machine but are unable to commence NIV due to lack of social care).

Date of first enrolment
01/05/2025

Date of final enrolment
30/04/2027

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Northern General Hospital
Herries Road
Sheffield
United Kingdom
S5 7AU

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
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John Radcliffe Hospital
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Study participating centre
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NR4 7UY

Study participating centre
Leeds Teaching Hospitals NHS Trust
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Study participating centre
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Study participating centre
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Sponsor type
Hospital/treatment centre

Website
http://www.sth.nhs.uk/

ROR
https://ror.org/018hjpz25

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC)

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal

Intention to publish date
31/01/2028

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.1	12/02/2025	07/04/2025	No	Yes
Participant information sheet	Intervention group version 1.1	12/02/2025	07/04/2025	No	Yes
Protocol file	version 1.1		07/04/2025	No	No