Trials

STUDY PROTOCOL

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Polysomnographic titration of non-invasive ventilation in motor neurone disease (*3TLA*): protocol for a process evaluation of a clinical trial

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Abstract

Background We are undertaking a multicentre randomised controlled trial to determine the effectiveness of including a sleep study (polysomnography (PSG)) to assist the commencement of non-invasive ventilation (NIV) in people with motor neurone disease (MND): the Polysomnographic titration of non-invasive ventilation in motor neurone disease (PSG4NIVinMND; *3-three letter acronym*; *3TLA*) trial. A process evaluation will be conducted alongside the clinical trial to understand: (1) the implementation of the *3TLA* intervention in the trial sites, including barriers and enablers, and (2) the mechanisms through which the *3TLA* intervention produces change. This protocol paper describes the rationale, aims and methods of the *3TLA* process evaluation.

Methods To guide the design of the process evaluation, a logic model representing the *3TLA* intervention, the likely mechanisms of impact, potential external contextual factors and assumptions, and the anticipated outcomes was developed by the researchers in collaboration with the 3TLA Trial Steering Committee. From this, five key process evaluation research questions were identified, a priori. The mixed-methods design is guided by three implementation frameworks: the Reach, Effectiveness, Adoption, Implementation and Maintenance (RE-AIM) framework, the Theoretical Domains Framework (TDF), and the Theoretical Framework of Acceptability (TFA). We will conduct semi-structured interviews with approximately 20–30 clinical trial participants (people with MND) and their carers, and focus groups and surveys with approximately 60 health professionals involved in delivering the intervention at each site. Quantitative process data will also be collected from the main clinical trial. Qualitative and quantitative data will be analysed iteratively throughout the trial, independent of the main trial outcome analyses. Process evaluation findings will be triangulated with the results of the clinical trial.

Discussion This process evaluation incorporates a mixed-methods design and is informed by three theoretical frameworks. It will provide insights into how the *3TLA* intervention was implemented, for whom and how the *3TLA* intervention was (and was not) effective, and what adaptations may be needed to facilitate future implementation into routine clinical practice.

Trial registration ClinicalTrials.gov NCT05136222. Registered on November 25, 2021.

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Background

Motor neurone disease (MND) is a rare and devastating neuromuscular disorder with a median survival of just 2 to 3 years from diagnosis. Respiratory failure from progressive muscle weakness is the most common cause of death [1]. Non-invasive ventilation (NIV) supports declining respiratory function and is currently the most effective therapy for extending survival in MND [2]. Until a cure is found, improving care for people living with MND by maximising the potential of NIV is essential.

Greater NIV usage per day better controls arterial carbon dioxide and reduces daytime sleepiness, with the 'effective dose' estimated at > 4 h/day [3]. In MND cohorts, survival is also improved in those who self-report using NIV for more than 4 h/day compared with either minimal or no use at all [4–7]. Despite the well-established benefits of using NIV to treat chronic respiratory failure in MND [8], uptake and usage of the therapy is extremely low. Australian registry data indicates that just 19% of Australians with MND access NIV [9]. Of those who do, approximately 45% use it for greater than 4 h per night [10]. Together, these data suggest that less than 10% of Australians with MND are adequately treated with NIV.

A complex array of interacting patient, health professional, and health system level factors influence the uptake and usage of NIV [11]. Those living with MND have reported a broad range of both positive and negative experiences with NIV. To the person with MND, NIV can represent hope and opportunity, but also cause anxiety, despair, and frustration. An adjustment to the person's identity is often required [12]. For health care providers, there is no universal consensus on how best to implement NIV in people with MND. Global clinical practices are variable, ranging from multi-night inpatient hospital admissions, ambulatory outpatient or home-based models [13, 14]. The inclusion of an overnight, polysomnographic sleep study (PSG) can be used to assess and subsequently align the ventilator settings to the patient's breathing. By undertaking the overnight PSG, clinicians can directly observe and respond to the patient-ventilator interaction, pulmonary gas exchange, respiratory drive, and sleep quality. Our team has provided the first randomised controlled trial (RCT) evidence that using a sleep study to assist with the commencement of NIV improves nightly usage by 118 min (95% CI 53–182, $p < 0.01$) compared with control. The single site study demonstrated a corresponding reduction in patient-ventilator asynchrony event rates, suggesting that optimising alignment of the patient's breathing with the ventilator is the causal mechanism for increasing the use of NIV [15]. We are undertaking a multicentre RCT to determine the effectiveness of PSG assisted commencement of NIV in MND: the *PSG4NIVinMND* (*3-three letter acronym*; *3TLA*) trial.

The protocol for the RCT has been described in detail elsewhere [16]. Briefly, *3TLA* is a two-arm, individual participant randomised controlled, assessor-blinded superiority trial in MND care centres across Australia. Eligible participants will be randomised on a 1:1 basis to either the intervention group (daytime and PSG assisted commencement of NIV settings; Intervention) or sham group (daytime commencement of NIV settings and sham PSG; Control). The primary outcome is the proportion of participants using NIV for > 4 h/day during the intervention period. Trial participants are adults with a clinical diagnosis of MND in whom NIV therapy is clinically indicated. The trial includes a health economic evaluation, including comparison of early costs of NIV care (related to health care contacts, equipment changes, adjustments, assessments during the intervention period) between groups using Medicare Benefit and Pharmaceutical Benefit Scheme data as described in the RCT protocol [16].

PSG assisted titration of NIV (the *3TLA* intervention) is a highly specialised intervention requiring experienced staff and specialised equipment in a dedicated facility. Delivery of this intervention requires substantial coordination between the patient, their family and carers, and the clinical team. Inherent to the intervention is an overnight stay in hospital which can be challenging for people with MND who are often experiencing a rapid decline in their function and multiple competing priorities. People with MND and their carers often experience profound feelings of grief and loss because of the progressive nature of the illness and can be overwhelmed with new information and health care appointments [17, 18]. Thus, the *3TLA* intervention may be perceived as a challenging addition to the usual NIV initiation process for patients and their carers. Similarly, with ever increasing demands on health professionals and health services, understanding how key stakeholders experience the intervention will assist with interpretation of the trial outcomes and future implementation efforts.

Process evaluations are increasingly conducted alongside clinical trials of complex interventions to understand for whom, how and why the intervention had a particular outcome. The purpose of a process evaluation is to help explain any variation in outcomes and to understand whether the intervention is acceptable and feasible to both the target population and those delivering the intervention. The UK Medical Research Council (MRC) has defined complex interventions are those with multiple interacting components. Interventions requiring substantial expertise and skills to deliver, targeting multiple behaviours, groups, and levels of the system, and/

or those with permitted flexibility in the delivery can all be considered complex [19, 20]. For the many reasons outlined above, the *3TLA* trial is investigating a complex intervention.

The MRC guidelines recommend that process evaluations of complex interventions include consideration of three key research questions, relating to implementation (*what is implemented and how?*), mechanisms of impact (*how does the intervention deliver change?*), and context (*what contextual factors affect implementation and how?*) [19]. Answering these questions facilitates interpretation of the trial outcomes, particularly when the results are not as anticipated or ambiguous. It also guides strategies for future implementation in real-world settings. Future implementation of this intensive model of initiating NIV in people with MND will require substantial practice change. PSG assisted commencement of NIV is not standard care in most Australian MND services, and anecdotally, the models of implementing NIV in people with MND vary substantially across the country. Thus, understanding the barriers and enablers to both delivering (health professional) and receiving (patient and carer) this new intervention is critical. A theory-based analysis of treatment implementation throughout the trial will enable the systematic identification and characterisation of strategies that target the causes of low usage of NIV. This paper describes the protocol for the process evaluation of the *3TLA* trial.

The aim of the *3TLA* process evaluation is to explore the factors that influenced implementation of the 3TLA intervention in MND centres in Australia and to understand how the PSG intervention led to changes in outcomes. The specific objectives are:

- To assess the implementation of the 3TLA intervention in the trial sites, including barriers and enablers
- To explore the mechanisms through which the PSG intervention produces change and identify any external contextual factors that may affect the delivery and impact of the PSG intervention

Methods

Project governance

Ethical approval for the process evaluation was obtained through the Austin Health Ethics Committee (HREC/68088/Austin-2021) alongside approval for the 3TLA trial. The comprehensive trial was registered on ClinicalTrials.gov (NCT05136222) on November 25, 2021.

The *3TLA* trial is governed by a Steering Committee, comprising all central and site investigators, and co-chaired by MND community organisation partners. The process evaluation will be overseen by the Implementation Committee, which will report progress and outcomes to the Steering Committee. The baseline and follow-up focus group guides, interview guides and questionnaires were drafted by two researchers from this committee and revised and ratified by the Implementation Committee. Researchers collecting and analysing the process evaluation data are not involved in the main trial analysis, nor the delivery of the trial intervention in any of the participating sites.

Design

The process evaluation is guided by the MRC framework for designing process evaluations of complex interventions in clinical trials [19, 20]. In accordance with MRC recommendations, a logic model was developed to summarise and define the intervention, the likely mechanisms of impact, potential external moderating factors and assumptions, and the implementation and participant outcomes (Fig. 1). To develop the logic model, the 3TLA trial management team and Process Evaluation team met on several occasions to discuss the mechanisms and assumptions of the intervention. Following these discussions, a draft logic model was designed. This draft was presented to the 3TLA steering committee for their feedback and input. After several iterations, the final logic model was approved by the Steering Committee.

From this logic model, we have identified the following key process evaluation research questions:

1. What is current practice of NIV initiation each site? How does this change throughout the trial?
2. What are clinician's beliefs, attitudes, and skills regarding the 3TLA intervention? What are the barriers and facilitators to delivering the 3TLA intervention?
3. How acceptable is the 3TLA intervention to people with MND and their carers?
4. How is the 3TLA intervention delivered at each site? (e.g. fidelity, quality, dose, reach)
5. What are the mechanisms of impact of the 3TLA intervention?

To address these research questions, the process evaluation will employ a mixed-methods design, comprising qualitative and quantitative data collection alongside the main trial (Fig. 2). Quantitative process data will be collated from the *3TLA* trial data. Qualitative data will be collected from semi-structured interviews with people with MND (trial participants) and their carers, and surveys and focus groups with health professionals involved in the clinical delivery of NIV for people with MND at each of the sites. The data plan and schedule for the process evaluation is summarised in Table 1.

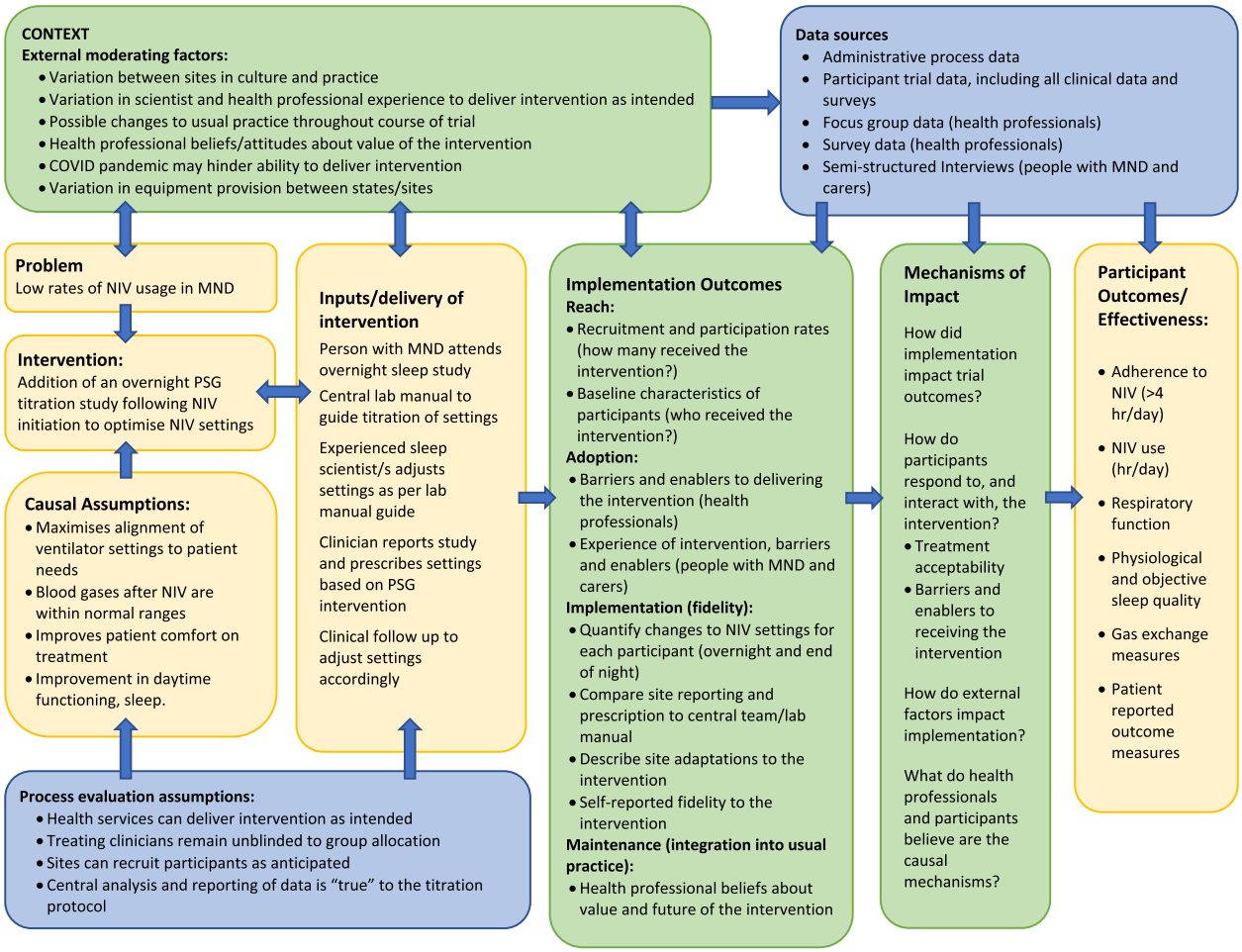

Fig. 1 Logic model

We will use three established implementation frameworks to guide the process evaluation: the RE-AIM framework [21], the Theoretical Domains Framework (TDF) [22] and the Theoretical Framework of Acceptability (TFA) [23]. The RE-AIM framework is designed to improve the sustainable adoption and implementation of effective, generalisable, evidence-based interventions and was selected because it covers the broad range of outcomes that are important for assessing the implementation of this trial intervention [21]. The TDF includes a validated set of 14 behavioural domains and is used extensively to explore factors (barriers and facilitators) that influence healthcare professional behaviours (research question 2) [22]. The TFA includes seven constructs to assess the extent to which people delivering or receiving a healthcare intervention consider it to be appropriate or acceptable [23]. Acceptability of a health care intervention is theorised to facilitate successful implementation [24]. The TFA was therefore selected to support research question 3.

Participant eligibility and consent

Health professionals

Health professionals from the participating trial sites who are involved in the delivery of NIV to people with MND will be invited to participate in the site-specific focus groups. Health professionals may include neurologists, sleep physicians and scientists, respiratory nurses, and physiotherapists. Written informed consent will be required before the focus group begins. Each focus group is anticipated to include approximately six to ten participants (~60 in total). We will seek representation from all disciplines that are involved in delivering the care model from each site, including a range of experience levels.

Similarly, all health professionals involved in the delivery of NIV to people with MND will be eligible and invited to complete an online survey. Eligible participants will be nominated by the principal investigators at each site. We anticipate that the survey will be distributed to approximately 60–70 participants (~8–10 from each 3TLA site). A participant information sheet is provided

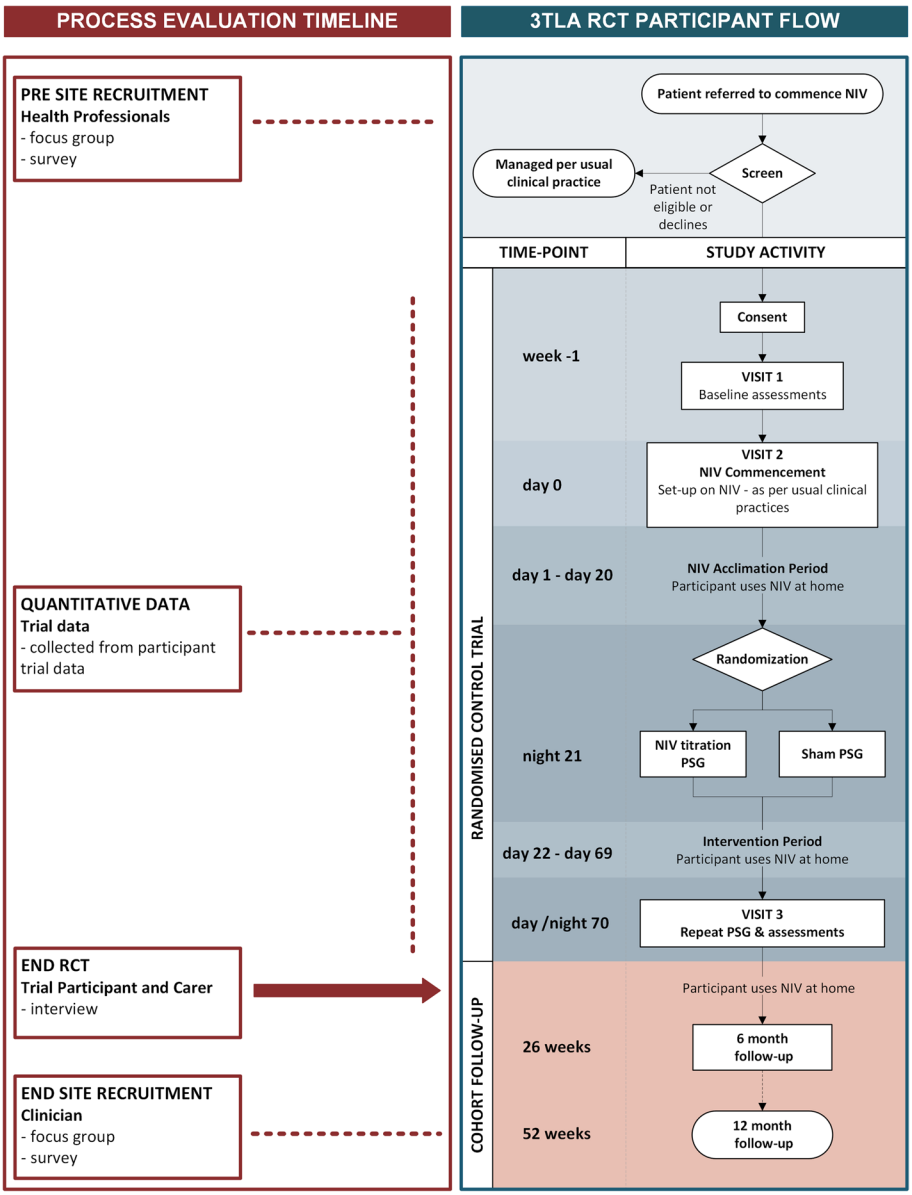

Fig. 2 Process evaluation

at the beginning of the survey which explains that by completing the survey, the health professional participants are consenting to their data being used for this research. Focus groups and surveys will be completed at two timepoints: before trial commencement and at the end of participant recruitment, with the surveys distributed following the focus groups.

People with MND and carers

The eligibility criteria for trial participants (people with MND) have been outlined elsewhere [16]. All trial participants (people with MND) will be required to provide written informed consent. Individual consent will also be obtained from carers of trial participants (people with MND) for the collection of outcome data during the intervention period. As part of this process, participants will consent to being contacted and invited to participate in a semi-structured interview. The researcher conducting the interviews will be informed by the site coordinator when a 3TLA trial participant is close to finishing the trial. Within a month of completing the trial intervention period, a sub-set of trial participants and carers will be invited to participate in a semi-structured interview to gain an in-depth understanding of their perceptions

Table 1 Process evaluation data plan

RE-AIM element	Research questions	Elements assessed	Data source/s	Timepoint/s
Reach	*How many received the intervention? Who received the intervention and are they representative of the target population?*	Intervention participation rates by site; baseline characteristics (medical specialist referral pathways, age, postcode, living situation, MND phenotype, etc.) of all participants	Trial data	Baseline enrolment
Effectiveness	*What effect did the intervention have on health behaviours and outcomes? Were there any positive, negative and unanticipated consequences?*	Behaviour: NIV usage (h/day), participant interaction with the service Outcomes: clinical outcomes, health-care utilisation, participant and carer questionnaires as their trial participation ends	Trial data	Baseline, end intervention period, 52-week review
Adoption	*Was the intervention acceptable and feasible to health professionals and participants?*	Acceptability, feasibility, uptake, enablers and barriers	Semi-structured focus groups and surveys with health professionals	Prior to trial commencement and at site intervention period completion
	What were the barriers and enablers to the intervention? How were they overcome?		Semi-structured interviews with participants and carers at trial end	Following the intervention period
Implementation	*Was the intervention delivered as anticipated? (Fidelity)*	Proportion of NIV setting changes made in response to patient and PSG data (control group)	Trial data	Intervention period
		Site vs central pre/post PSG changes in NIV settings (intervention group)		
		Self-reported fidelity	Health professional focus groups	At site intervention period completion
Maintenance	*Will the intervention be maintained following the trial?*	Health professional opinions and beliefs about value and future of the intervention	Health professional focus groups and surveys	Prior to trial commencement and at site intervention period completion
		Changes to process measures (e.g. time to NIV initiation; type and frequency of follow-up support)	Trial data	Intervention period

NIV non-invasive ventilation, *PSG* polysomnography, *RCT* randomised control trial

and experience of the NIV initiation process and subsequent use of NIV. Within the same family, interviews will be conducted with the person with MND or their carer, though the interviewee can choose to have the other person present in the interview. This flexible approach has been chosen to recognise the important role of carers for people living with MND and to support the participant's choice in who they would like to be present during the interview.

A purposive sampling technique will be employed to ensure a mix of participant demographics (gender, age, carer vs patient) and trial sites. To ensure adequate diversity, the demographic characteristics of potential participants will be considered in relation to those who have already completed an interview. If the participant accepts the invitation to the interview, a participant information sheet explaining the study will be provided, and verbal consent will be audio-recorded prior to commencement of the interview. We anticipate recruiting between 10 and 16 trial participants (people with MND) and 10 and 16 carers, with at least one carer and one person with MND from each of the seven 3TLA trial sites. Justification for this sample size estimate is provided in the Data analysis section.

Data collection procedures—qualitative and survey data

Health professionals

Focus groups will be conducted at two timepoints related to the clinical trial: before trial commencement and in the final year of trial recruitment. The purpose of the focus groups is to obtain an in-depth understanding of the NIV initiation practices at each site and whether this changes over the course of the clinical trial, as well as the health professionals' expectations (baseline) and experiences (follow-up) of delivering the trial intervention. Focus groups will be conducted by an experienced implementation researcher, supported by a second researcher, and conducted face to face or via videoconferencing at a suitable time for each clinical team. Researchers conducting the focus groups are implementation science experts who have not worked clinically in any of the participating sites. Researchers will ensure that all participants have an equal opportunity to contribute their opinions by actively monitoring the conversation and encouraging quieter participants to respond. Focus groups will be audio-recorded to allow for transcription and analysis of results. All discussions and responses will be de-identified to ensure clinicians and sites cannot be identified from their responses. The semi-structured interview guide is provided in Additional file 1: Clinician focus group guide.

Surveys will be completed following the focus groups at the same two timepoints: before trial commencement and in the final year of trial recruitment. The survey, based on the TDF, aims to understand the barriers and enablers to undertaking the PSG intervention and how their views and practice may have changed throughout the trial period. It includes demographic questions such as professional background, years of experience, and role in the NIV service, followed by a series of questions aiming to understand the barriers and enablers to the PSG intervention. These questions require 7-point Likert scale responses, indicating level of agreement with various statements that are based on the 12 domains of the TDF. In the follow-up survey, participants are asked to provide feedback on aspects of the clinical trial and written, qualitative responses on the barriers and enablers to delivering the PSG intervention. The survey will be circulated to all members of the clinical team involved in the management of NIV in people with MND at each site. No identifying information will be collected, though health professionals will be asked to provide basic demographic information and a personalised 'code' so that their baseline and follow-up data can be linked. The research team will not be able to identify participants from their personalised code. The survey questions are provided in Additional file 2: Clinician survey.

People with MND and their carers

Participants who consent to the interview will be interviewed by an experienced researcher who is not involved in the participant's routine care. Interviews will take place at a time and location (including telephone/videoconference and face-to-face where possible) of the participant's choosing. Interviews will be audio-recorded to allow for transcription and analysis of results. Interpreters will be offered for people who do not speak English as their first language. Where a participant is non-verbal, the option of providing written responses to interview questions (e.g. by typing or using their usual assistive technology) will be offered. Implementation of NIV can be stressful, and each site has support structures in place as part of their usual clinical care. Should any participants experience distress during or after the interview, the investigators will arrange appropriate counselling through services unrelated to the trial. If carers report distress associated with their caring responsibilities, the research team will report this to a member of the clinical team within 24 h for further follow-up/referral to counselling services. Sampling will continue for both patient and carer groups until data saturation is reached where no new themes emerge from the data. This is defined as a minimum of 10 interviews in each group, with an additional three participants recruited until no new themes emerge from the additional data [25]. The participant and carer semi-structured interview guide is provided in Additional file 3: Participant interview guide; carer interview guide.

Data collection procedures—quantitative data

Quantitative data will be collected and recorded from participants at each site throughout the trial. As part of the process evaluation, we will extract and analyse the following participant trial data:

- Participant demographic and medical information, including site, age, sex, residential remoteness, state of residence, living situation, MND phenotype and time since MND diagnosis
- Overnight adjustments to NIV settings during PSG titration study (vs without PSG)
- Recommended 'end of night' changes to NIV settings (clinician vs central trial recommendations)
- Service use in the intervention period (rate and type of review appointments)
- Participant NIV usage data throughout the trial (hours per 24-h period, commencing at 12:00 pm)
- Other NIV device derived indicators including unintended mask leak, estimated ventilation and apnoea hypopnoea index
- Change in participant reported outcome measures

Data management and storage

The management and storage of trial data have been reported in the 3TLA trial protocol. The audio-files for all focus groups and interviews will be destroyed following verification of accurate transcription. Transcribed interviews and focus groups will be stored in a password-protected folder, accessible only to the researchers, and maintained in accordance with the Public Record Act 1973 (Victoria), the Austin Health information Security Policy, The University of Melbourne Research Data Management Policy and relevant privacy legislation. The data will be kept indefinitely. If information or data are destroyed, it will be destroyed in a secure manner that protects the privacy and confidentiality of this information.

Intervention fidelity

Assessment of intervention fidelity will allow for the inherently flexible intervention. Fidelity with the standardised components of the intervention will be assessed (e.g. timing of 3TLA intervention, blinding to group allocation). We will also estimate the quality of the intervention delivery and the variation between sites, using qualitative and quantitative methods. Health professionals will be asked to provide their opinions about the quality of the intervention delivered at their site during the second rounds of focus groups. Quality and dose of the intervention will be assessed quantitatively using two methods described in Table 2. The proportion of overnight NIV setting changes made in response to the participant and the PSG data will be calculated in the control group to assess fidelity with the protocol. All PSG studies will be sent to the central trial team for review where a clinician expert will independently report the study and make recommendations to the settings. These centrally made setting recommendations will be used to assess quality of the PSG intervention at each site and variation between sites. The central recommendations will not be disclosed to the sites. The absolute changes to all NIV settings between the 'end of night' and 'beginning of night' prescriptions will be compared to those recommended by the central team. Self-reported fidelity will also be collected in the surveys and focus groups with health professionals at the follow-up timepoint.

Table 2 Intervention fidelity assessment plan

#	Measure	Description	Data
PSG titration fidelity (control group)			
1	Proportion of NIV setting changes in response to participant and PSG data	The expectation for this component of the fidelity assessment is that 100% of the changes made to NIV settings in control group participants are in response to the participant reporting issues overnight. This will be evidenced by text notes (and subsequent setting changes) within the PSG data files	Count and type of NIV setting changes during baseline PSG Count and type of NIV setting changes in response to patient complaint and PSG data
NIV prescription fidelity (intervention group)			
2	Difference in absolute changes to NIV settings (pre/post PSG) between the sites and the central team	A comparison of the magnitude of the change in NIV settings from pre to post PSG between the site and central prescription i.e. difference in site vs central pre-post change in inspiratory positive airway pressure/expiratory positive airway pressure, etc	Pre-PSG (beginning of night) NIV prescription (all settings) from site Post-PSG (end of night) NIV prescription (all settings) from site and central team

Data analysis

Qualitative data (people with MND, carers, health professionals)

Interview and focus group data will be transcribed verbatim using a professional transcription service. Researchers will check the transcripts for accuracy against the recordings, and any identifying information will be removed prior to analysis. Analysis of participant interviews, focus groups, and qualitative responses to surveys will be analysed using a deductive approach to framework analysis [26], using the TDF constructs to ascertain barriers and enablers to implementation, and the TFA constructs to explore acceptability and adoption of the 3TLA intervention. Analysis and interpretation of the findings will be relevant to the objectives and research questions defined in the logic model (Fig. 2). Inductive identification of themes will also occur if relevant data is identified that does not fit within the constructs of the TDF and TFA, or if greater context is needed for interpretation of the barriers and facilitators identified in the deductive analysis. Data will be thematically analysed by an experienced qualitative researcher. This approach to data analysis will produce theory-driven pragmatic findings that can be used to inform practice change, whilst ensuring that the perspectives of participants remain central to the analysis [27]. Data coding and analysis will be conducted by an experienced qualitative researcher, with 10–20% of interview transcripts independently coded by another researcher. These researchers will then meet to compare their initial coding, to resolve conflicts through discussion, and to agree on a coding framework for the remaining data. Interpretation of the findings will be conducted by a team of researchers (led by MG) and discussed with the Steering Committee.

Survey data (health professionals): Surveys will initially be analysed separately from the focus groups. Quantitative survey data will be analysed descriptively and reported as counts/proportions and measures of central tendency and dispersion, as appropriate. Qualitative responses will be analysed thematically using the TDF domains to identify barriers and enablers to the PSG intervention. Themes and findings of the qualitative and quantitative components of the survey will then be combined and compared to identify agreements and discrepancies. Following this, focus group results will be integrated with the survey findings to identify major influences on the delivery of the 3TLA intervention.

Quantitative data (participant trial data): Clinical trial data will be analysed descriptively to report information on the delivery of the intervention, in accordance with the RE-AIM framework (see Table 1) and logic model (see Fig. 2). Counts and proportions, and measures of central tendency and dispersion (means and standard deviations or medians and interquartile ranges) will be reported as appropriate. Differences in the delivery (e.g. time to PSG1, fidelity, type and frequency of follow-up support) of the intervention by relevant factors (e.g. site, MND phenotype, age group) will be assessed with statistical tests comparing measures of central tendency (e.g. independent *t*-test, ANOVA, Kruskal–Wallis) or counts/proportions (e.g. chi-squared test), as appropriate. Differences in absolute changes to NIV settings (pre/post PSG intervention) between the sites and the central team will be presented graphically in Bland–Altman plots and the 95% limits of agreement will be reported.

Mixed methods analysis

Qualitative and quantitative data analyses will initially occur separately according to the protocol described above. Upon completion of the 3TLA trial, all results will then be combined and analysed together using a method of data triangulation. An integrated visual display containing findings from both the qualitative and quantitative analyses will be developed and mapped to the process evaluation logic model (Fig. 2) [28]. This process of integration and comparison will enable researchers to identify where there is agreement and dissonance in findings and to estimate the strength and importance of the various findings. The mixed methods analysis will be used to assess the implementation outcomes and the mechanisms of impact; identify external moderating factors impacting the study results; and assist with interpreting the outcomes of the trial.

Integration of findings

The process evaluation and the main *3TLA* trial analyses will be completed independently. The process evaluation will occur iteratively and throughout the duration of the clinical trial and be executed by the process evaluation researchers (led by MG) who will not be involved in the analysis of the clinical trial (led by DB). The process evaluation researchers will not inform the researchers and statisticians involved in the analysis of the main trial data of the findings of the process evaluation until after the main outcomes of the clinical trial have been analysed. When both analyses (main trial and process evaluation) have been completed, the results will be integrated to assist the trial investigators to understand and interpret the findings of the trial, particularly if the analysis of the primary outcome provides results that are ambiguous or unanticipated, or if the intervention was found to be more effective in some groups or settings than in others. This information could lead to new hypotheses about causal mechanisms, mediators, and moderators of the intervention, and post hoc testing of these hypotheses may be conducted.

Discussion

This process evaluation aims to complement and enhance the evaluation of the 3TLA trial comparing an intensive method of NIV initiation in MND to usual care. It involves the collection and analysis of quantitative and qualitative data from a wide range of stakeholders, including trial participants (people with MND), their carers, and the health professionals involved in delivering the intervention. This comprehensive approach will facilitate a holistic understanding of the determinants of the intervention and its mechanisms of impact.

The process evaluation has been designed to explore the determinants of successful implementation of the *3TLA* intervention for the sites involved in the trial. Should the clinical trial conclude that the intervention is effective, this information will facilitate the development of a targeted implementation strategy for future application in hospitals across Australia and elsewhere. The process evaluation will also assist with understanding for whom and how the *3TLA* intervention was impactful, and which components of the intervention were the most likely to contribute to the outcome.

Trial status

- Protocol version 2.1 dated 12 March 2024 (RCT protocol); Ethics Addendum version 3 dated 18 August 2023 (process evaluation protocol).
- Trial recruitment commenced 15 December 2021; the process evaluation recruitment commenced 23 September 2021 with the first site focus group.
- As of 25 August 2023, baseline focus groups and surveys had been completed with health professionals from all seven trial sites and analysis has commenced.
- Interviews with trial participants (people with MND) and their carers commenced 22 February 2023. Iterative analysis of qualitative interview data has commenced.
- The trial was powered to cease recruitment when 244 participants were randomised and scheduled to be completed in 2026. Trial commencement was delayed by 18 months due to the COVID-19 pandemic. These delays have significantly impacted recruitment and trial completion timelines.

Abbreviations

3TLA	Polysomnographic titration of non-invasive ventilation in motor neurone disease trial
TDF	Theoretical Domains Framework
TFA	Theoretical Framework of Acceptability
MRC	Medical Research Council
MND	Motor neurone disease
NIV	Non-invasive ventilation
PSG	Polysomnography
RCT	Randomised controlled trial
RE-AIM	Reach, Effectiveness, Adoption, Implementation and Maintenance

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13063-025-08784-z.

Additional file 1. Focus group guide—clinicians. Semi-structured focus group questions based on the Theoretical Domains Framework and the Theoretical Framework of Acceptability to obtain an in-depth understanding of the NIV initiation practices at each site and whether this changes over the course of the clinical trial, as well as clinician's expectations (baseline) and experiences (follow-up) of delivering the trial intervention.

Additional file 2. Clinician questionnaire. A survey for clinicians involved in the 3TLA trial, based on the Theoretical Domains Framework, to understand the barriers and enablers to undertaking the PSG intervention and how their views and practice may change throughout the trial period.

Additional file 3. Interview group guide—participant and carer. Semi-structured interview questions based on the Theoretical Domains Framework and the Theoretical Framework of Acceptability to gain an in-depth understanding of their perceptions and experience of the NIV initiation process and subsequent use of NIV.

Additional file 4. SPIRIT checklist for Trials.

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Authors' contributions

The process evaluation protocol was developed by all authors. MG led the preparation of the manuscript. All authors reviewed contributed to the manuscript and approved the final version prior to submission.

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Data availability

In accordance with recommendations of the International Committee of Journal Editors, individual participant data will be retained and shared. Pseudonymised data will be available with no end date to selected trial researchers along with a separate password-protected dataset linking trial identifiers to trial participants. Participants will be provided with a summary of the results of the main trial and process evaluation components. The results of the study will be disseminated in presentations and publications without restriction. Anonymised individual participant data that underlie the results reported in publications will be stored in a secure online repository, beginning 9 months following publication with no end date [29].

Ethics approval and consent to participate

Ethical approval for all sites has been granted by Austin Health Human Research Ethics Committee (HREC/68088/Austin-2021). Informed consent to participate will be obtained from all participants. Any proposed amendments to the project including any changes to the protocol, participant information and consent form/s, agreed upon by the Trial Steering Committee, will be submitted to the reviewing HREC for approval prior to implementation. These changes will be communicated to the trial participants by members

of the research team and re-consent for participation in the research will be collected if required.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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