Full-Length Article

Exploring the Feasibility of a Music-assisted Relaxation Intervention to Assist Initiation of Non-invasive Ventilation in People with Motor Neuron Disease

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Abstract

Background: The process of transitioning to non-invasive ventilation (NIV) can be anxiety provoking for people with Motor Neuron Disease (MND), and this may reduce adherence rates. Music therapy has demonstrated positive effects for patients receiving mechanical (invasive) ventilation, such as reducing blood pressure, respiratory rate, and anxiety.

Method: This feasibility study examined the effects of music-assisted relaxation (MAR) on NIV adherence, anxiety, and quality of life for people with MND. Data were collected at baseline, 7-days post, and 3-months post NIV implementation.

Results: Of 18 consenting participants, 15 chose the MAR condition. Results suggested that supporting NIV transition within the first 7 days could be advantageous for long-term adherence. Although these results did not show quantifiable results for anxiety or quality of life, the effect on adherence could have implications for these domains in the future as adherence may instil resilience. Limitations included small sample size, lack of an adequate control, and possible ceiling effects on the instruments used. Qualitative data indicated most participants considered the relaxing and distracting effects of MAR were useful.

Conclusions: In this small sample, we found some demand for and acceptability of a music-based intervention in this setting. Participants reported differing experiences of using MAR, and there were technical and logistical issues regarding timely and accessible provision of a MAR intervention within the treatment trajectory of NIV implementation. Conflicting quantitative and qualitative data support the need for mixed method research in this area.

Keywords: ***music therapy, relaxation, non-invasive ventilation, motor neuron disease, amyotrophic lateral sclerosis***

multilingual abstract | **mmd.iammonline.com**

Introduction

Motor Neuron Disease (MND), also known as Amyotrophic Lateral Sclerosis (ALS)[1], is a non-curable degenerative disease whereby the motor neurons progressively degenerate and overtime die. The incidence of MND is approximately 2 in 100,000[1], with an average onset of about 60 years of age [2] and typical life expectancy of 3-5 years post diagnosis [3]. Regardless of the type or origin of MND, the disease eventually affects all motor neurons. When the inspiratory muscles are no longer able to undertake adequate ventilation, oxygenation to the body is compromised, leading to death.

Non-invasive ventilation (NIV) is recommended to increase survival, improve symptoms and maintain quality of life as physical function declines with MND progression [4]. Inadequate or inefficient breathing causes breathlessness, sleep disruption, restless and unrefreshing sleep, headaches, excessive daytime sleepiness and lethargy, fatigue and poor appetite [5, 6]. Conversely, supporting ventilation with NIV not only improves survival but also increases quality of life [7] and cognitive function [8].

NIV works to combat respiratory inefficiency by pumping air directly through the mouth to open airways and allow air to be inhaled and exhaled [4]. NIV may reverse the chronic respiratory muscle fatigue by reducing a person's effort, which in turn improves oxygenation and cellular metabolism. NIV may also reverse hypercapnia (thereby improving respiratory drive) and atelectasis by inflating the lungs and in doing so improving lung compliance [3]. A recent Cochrane review indicated that NIV significantly prolongs life in people with MND by an average of 48 days, and 205 days for those with

1 Although MND is the widely used generic term in the United Kingdom, Australia and parts of Europe, ALS is used more generically in the United States, Canada and South America - http://www.alsmndalliance.org/what-is-alsmnd/

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mild to moderately impaired bulbar function [9].

Despite the documented benefits of NIV, up to 30% of MND patients do not successfully transition to regular NIV use and stop using it for a range of physical [10] and psycho-emotional[11] reasons (Figure 1). Some people with MND were concerned with becoming dependent on NIV and discontinued before they were able to realize its benefits [6], while others discontinued use because it failed to manage their symptoms or they were unable to adapt to the ventilated experience[12]. While it has been established that respiratory difficulties in MND are exacerbated by anxiety[13] and anxiety around NIV use is reported by patients with chronic obstructive pulmonary disease[14], it is unclear whether anxiety plays a role in NIV uptake in MND patients. Figure 1 depicts the physical and psycho-emotional risk factors influencing NIV uptake.

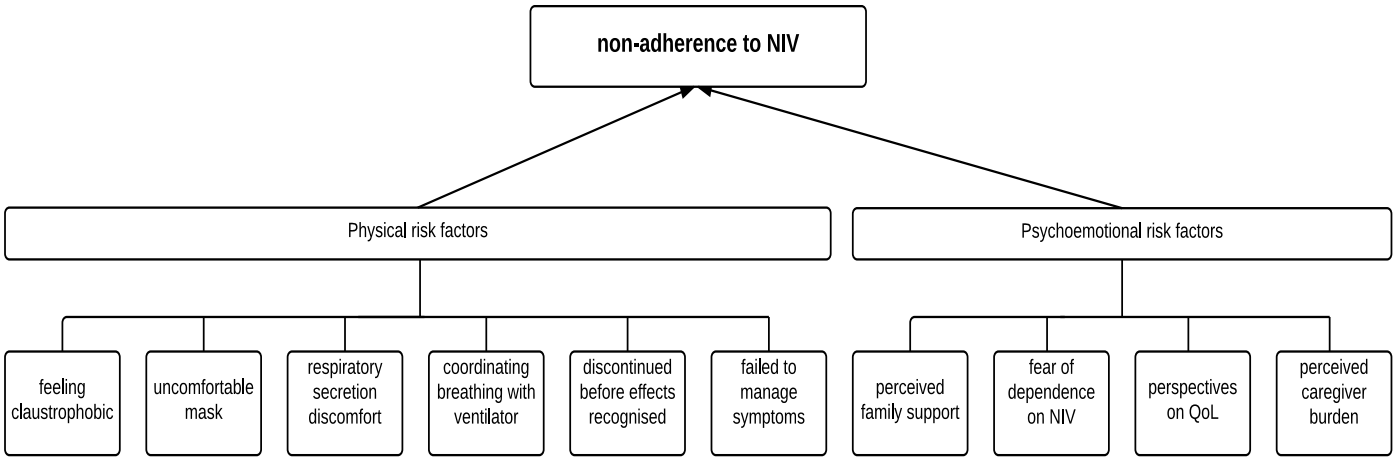

Figure 1. Physical and Psycho-emotional risk factors associated with NIV uptake.

To date no research has specifically addressed the psycho-emotional issues that may cause poor NIV uptake. Music-assisted interventions have the potential to address both physical and psycho-emotional issues associated with MND and transitioning to NIV. Music therapy has been shown to reduce anxiety in multiple sclerosis [15], preoperative contexts[16], burns dressings[17], and dental procedures[18].

Several studies have explored the use of music listening with people who are mechanically ventilated [19-24]. A recent Cochrane review[25] identified 14 studies (with 805 participants) where music listening significantly reduced anxiety during mechanical ventilation, and the effects were large and clinically significant. Music listening also reduced respiratory rate and systolic blood pressure, suggesting a relaxation response.

It is vital in a progressive disease such as MND that supportive interventions like NIV are implemented in a timely manner with maximal uptake. If not, the burden of the therapy may outweigh the benefit. Music listening may provide an accessible and non-invasive way for people with MND to manage the physical and psycho-emotional demands associated with successful NIV uptake. Music with a slow steady beat could decrease physiological stress responses and assist with unconscious entrainment to the ventilator respiratory rate [26]. Music may also help to mask the noisy sounds of the respirator and assist sleep onset and maintenance. Further, participant-selected music can be a positive stimulus to focus on [27, 28], promoting trust and offering an aesthetic experience of comfort and peace in times of distress [25].

Music listening can also affect people at the neurophysiological level via the sympathetic nervous system. Here, music is understood as having anxiolytic effects, suppressing the sympathetic nervous system activity, and in doing so, reducing the release of the stress hormone adrenaline [25, 29]. Music also activates the limbic system, releasing endorphins that contribute to an improved feeling of wellbeing [19]. Music listening has also been demonstrated to decrease the amount of sedation required during medical procedures [30-33]. This evidence further supports the relaxation response experienced through music listening. Another benefit of music in the NIV transition process is that if set up appropriately, it can be self-administered by a person with MND. This could create a feeling of empowerment, safety, and control because a person can decide when music is needed.

Prior to launching into a clinical trial to determine the effectiveness of a music intervention on NIV transition for people MND, feasibility issues need to be investigated [34]. Accordingly, we chose to explore several areas of focus for feasibility studies in this study: *acceptability, demand, implementation, practicality, adaptation, integration,* and *limited efficacy*. [35]

Study aims and research questions

The aim of the study was to collect feasibility data on NIV uptake and adherence and test the effects of a music-assisted relaxation (MAR) intervention protocol on selected wellbeing indicators and NIV usage data of people with MND. The research questions addressed were: 1) what is the uptake rate of MAR when offered to people with MND transitioning to NIV? 2) does MAR assist the transition from independent breathing to NIV in MND? 3) what is the experience of people with MND using MAR during transition to NIV? 4) what are the challenges to conducting research in the MND population?

Materials and Method

Study design

The study used a prospective, cohort design with baseline, 7-day, and 3-month assessments to track NIV use, and changes in anxiety and quality of life during the implementation period (first 7 days) and during the first 3 months. Participants were not randomly allocated to conditions for this feasibility trial. Rather, all participants had the option to select the MAR intervention or standard care (control condition) and provided informed consent to participate. The study was reviewed and approved by Human Research Ethics Committees at The University of Melbourne (1341021), Calvary Healthcare Bethlehem (13121302) and Austin Health (HREC/13/Austin/201).

Participants

All MND patients who were seen by the Victorian Respiratory Support Service (VRSS) over a 12-month period were assessed for eligibility to participate in this study. Inclusion criteria were: diagnosis of MND, sufficient English to complete the research measures, and referral for NIV implementation. Patients already using NIV were ineligible to participate.

Conditions

The MAR intervention began with an assessment with a registered music therapist (author 4) prior to NIV implementation to determine the participant's musical preferences and functional abilities (e.g. the capacity to start/stop music independently) and provide a trial relaxation session. The music tracks offered were selected by the music therapist for their anxiolytic and sedative properties based on theories of the regulating effect of music on physiological and emotional responses [36, 37] and were deemed conducive to facilitating a relaxation response.

Initially, 6 playlists of approximately 30 minutes in length were created within five genres: Classical (2 playlists), Celtic, Nature, Ambient and Popular. These categories are subjective but served as a way to systematically present music options to participants. The original Classical playlists included instrumental piano, guitar, and/or orchestral music from composers such as Chopin, Bach, and Brahms. The Celtic playlist included tracks from 'The Secret Garden' soundtrack and other similar Celtic music and was also predominantly instrumental. The Nature playlist included an assortment of Tony O'Connor tracks, and the Popular playlist included instrumental versions of various popular songs mainly from the 1970's. Participants were able to request other specific styles of music and/or specific pieces that were not included in the original playlists, such as Operatic and Classical guitar. Additional tracks were selected and added to individualized music playlists when required.

The music therapist played some of the tracks from each playlist to give each participant a taste for the music in each genre and sought feedback on whether the music was perceived to be relaxing. Some participants wanted to listen to every track to make sure they found each one relaxing. It is important to note that some participants found particular tracks too emotionally evocative due to their pseudobulbar affect[2] so it was important that each track chosen was suitable. Individualized music playlists were created by the music therapists based on the personal preferences of each participant. Some participants were happy with the overall feel of selected pieces in one of the genre-based playlists devised by the music therapist and opted to select one of these pre-existing playlists. Some participants preferred their individual playlist to be mixed-genres, and some preferred a single genre per playlist. The combination of music therapist-advised, participant-selected music worked well in this feasibility study.

The music used was not limited to a specific tempo but was selected based on the music therapist's knowledge of the sedative qualities of music, i.e. slow tempo, flowing melody line, minimal dissonance, predictable harmonic progression. All playlists were tested by the music therapist during individual music and relaxation sessions to ensure appropriateness. Individual playlists were arranged with the iso principle in mind [38], with slower, simpler, more sparsely textured music towards the end of the playlist and smooth transitions between tracks. Some patients requested more 'upbeat' music and stated that they didn't particularly like any of the styles of music offered. These participants were advised to try sedative music for the purpose of relaxation but were

[2] **Pseudobulbar affect** refers to **emotional lability** characterized by involuntary or uncontrollable episodes of crying and/or laughing, or other emotional displays that occurs secondary to a neurologic disorder or brain injury.

given the option of one CD with their requested upbeat music playlist and one with sedative music and advised to try both and find out which they felt was more effective.

Participants were provided with CDs containing their music playlists. During the initial assessment, the music therapist explored the best way for each participant to listen to his/her music. Most used their own CD player at their bedside or transferred the music from the CD onto their own mp3 player. One participant was loaned a CD player and an mp3 player. One participant requested that the music be transferred to a USB stick so they could upload it themselves to their own device.

The music therapist verbally debriefed with each participant at the end of the initial assessment session, looking for any adverse reactions (i.e. some participants found particular pieces of music unpleasant, not relaxing, or too emotionally evocative). The debriefing content comprised discussion of the following aspects: how the participant found the experience of MAR; how it compared with previous relaxation experiences; how they felt the music affected them (particularly if they had chosen music that was different to what they would usually listen to); and whether they wanted to make any adjustments to their music choices after experiencing MAR. Participant preferences for music selections and length of the relaxation session were discussed and adjustments made to the final program of music as required. In the days following the assessment, the music therapist provided two final MAR programs (approximately 20-30 minutes in length) to the participant for use at home. Participants were asked to play the MAR programs via speakers at their bedside at a comfortable volume at night when they were trialling NIV and to keep the music playing until the end of the program. MAR participants kept a checklist of their music use. This involved ticking 'yes' or 'no' regarding whether they had used music each day for 14 days. Participants in the standard care condition were not provided with any music for use at home and attended their NIV implementation session as per the VRSS service protocol.

Outcome measures

NIV adherence was the primary outcome for this study and was extracted from routinely collected data measured by the NIV device on SD cards. Adherence data collected at 7-days and 3-months comprised: a) number of days NIV was used, b) number of hours NIV was used per day, and c) number of days used for >4 hours. Adequate adherence to NIV was defined as at least 4 hours per night on 5 of 7 nights per week [39, 40].

Secondary outcomes were quality of life and anxiety. Participants completed the Assessment of Quality of Life-8D (AQoL-8D) [41], a 35-item, generic quality of life measure with good reliability and internal consistency [42, 43]. Higher scores equate to a worse health-related quality of life).

Participants also completed the Hospital Anxiety and Depression Scale (HADS) [44], a 14-item assessment of anxiety and depression with good reliability and validity data across a range of populations [45] that has been used in previous music therapy studies of people with MND[46]. ThAmyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS –R) [47] is routinely used to assess the level of disability in people with MND and served as an indicator of disease severity and progression. The physiotherapist involved in NIV implementation provided a clinical judgment of the participants' likelihood of NIV adherence at the end of the implementation session using a 5-point Likert scale.

We conducted interviews with participants at 7-days post NIV implementation to explore the reasons participants chose the MAR or the standard care conditions, to determine how they found the NIV transition period, their experience of using NIV with or without the MAR, and any perceived changes in anxiety. Figure 2 outlines the procedure and data collection steps for all participants.

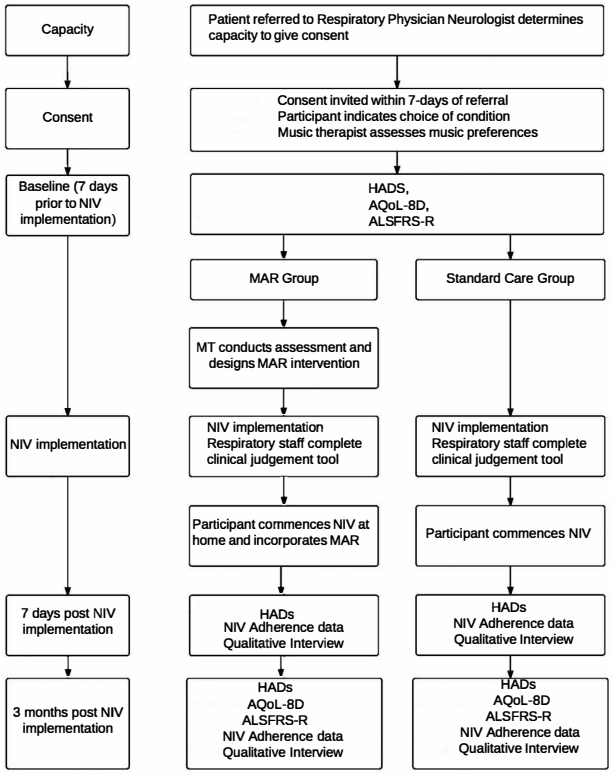

Figure 2. Flowchart of data collection procedures

Analysis

Descriptive statistics were calculated for all variables. Due to the non-randomised nature of the trial design, no group mean comparisons were planned. Additionally, analysis of longitudinal research in MND is typically complicated by

incomplete follow-up attributable to variable but often rapid decline in functional status. We performed paired Student t-tests for comparison of baseline with immediately subsequent (7-day or 3 months depending on the variable) measures and a repeated measures analysis of variance for outcomes with three time points. No attempt was made to construct linear models or to impute missing values to account for missing data because it was unlikely that such data would be missing at random.

Results

Participant recruitment

Figure 3 outlines the recruitment and retention rates of participants. Reasons for declining participation in the study were: 1) already participating in another study, 2) 'too much' for patient to consider at the same time as NIV implementation, and 3) clinical decision not to introduce the study because the patient's clinic appointment was distressing.

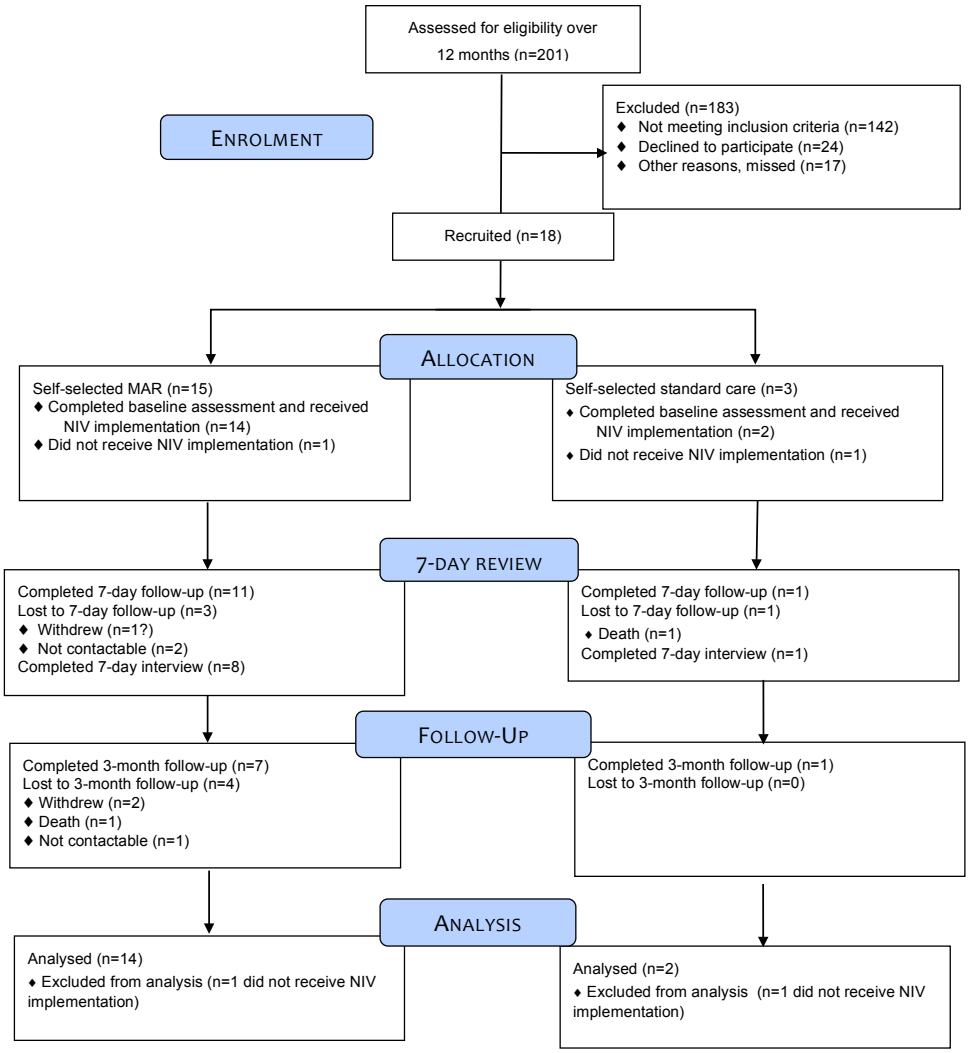

Figure 3. CONSORT flow diagram

Participant demographics

The final cohort of 16 participants was predominantly male (75%) and as anticipated, respiratory function was significantly compromised (table1). For the eight participants with 3-month ALSFRS-R data, disease severity remained fairly stable for four participants, but worsened by 6-11 points for four participants. The mean decrease of 4 points in ALSFRS-R scores for the cohort was not statistically significant (p= .09), however a change of 4 points on the ALSFRS-R indicates a clinically significant change[48]. A range of MND phenotypes were represented: cervical (n=2), lumbar (n=5), bulbar (n=5), cervical/flail limb (n=1), upper limb (n=2), and unknown (n=1).

Table 1. Baseline cohort demographics

Baseline demographics	Mean	Range
Age (years)	60	40-74
Time since diagnosis (months)	20	3-36
ALSFRS-R (score)	31	15-27
FEV_1 (litres)	2.03	0.72-3.25
FVC (litres)	2.57	0.69-3.92
MEP (cm/H_2O)	50	21-86
MIP (cm/H_2O)	34.4	0-60
SNIP (cm/H_2O)	37.2	17-57

Abbreviations: ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised; FEV_1, Forced Expiratory Volume in one second; FVC, Forced Vital Capacity; MEP, Maximal Expiratory Pressure; MIP, Maximal Inspiratory Pressure; SNIP, Sniff Nasal Inspiratory Pressure

Missing data

13 MAR and 2 SC participants completed the HADS and AQoL at baseline. 10 MAR and 1 SC participant completed the HADS at 7 days and 8 MAR and 1 SC participant completed the 3 month assessments for both HADS and AQoL. NIV usage data however, was more consistently collected although one SD memory card was returned blank, and one SD card was broken in the post. NIV usage data were available for 9 of 16 participants at both 7-day and 3-month time points. Reasons for missing NIV data at 7-days were illness/death (n=5) and equipment malfunction (n=1, this participant did have usage data at 3 months). At 3-months two more participants had withdrawn due to ill health.

Research question 1 – What is the uptake rate of MAR when offered to people with MND transitioning to NIV?

Of the 14 participants who commenced MAR, 8 used it, 4 did not and 2 withdrew before 7-day data collection was completed. All participants completed the music listening checklist, except the 2 who withdrew. Some participants used MAR regularly (n=3), one intermittently, and others used it after technical difficulties were addressed (n=4). Technical difficulties included difficulties using a CD player (due to cognitive impairment, n=1), setting up a CD player at bedside, or not having the MAR CDs yet. Other issues regarding copyright and syncing arose when participants wanted the music in digital format to use on a personal listening device. Reasons for not using MAR included not needing the extra support after commencing NIV (n=2), or conversely having difficulty with the NIV transition and not wanting to add a further intervention (n=2). The checklist of music use data over the first two weeks showed that three participants achieved optimal MAR use (> 5 days/week), two achieved partial MAR use (3-4 days/week) and one only used MAR twice per week. A further two MAR participants used the intervention at 4 and 6 weeks after initial technical difficulties.

Research Question 2 – Does MAR assist the transition from independent breathing to NIV in MND?
NIV adherence

At the 7-day review, 8 of the 10 participants with NIV usage data had used NIV every day, however only 7 of these had achieved NIV adherence as previously defined. Of those with 3-month NIV data, all six participants who achieved adequate adherence to NIV at 7-days maintained this at 3-months. The three participants who had not achieved adequate adherence at 7-days persisted with NIV, but were not adherent at 3 months. The physiotherapist predictions for who would achieve adequate adherence at 7 days were not accurate

When comparing the NIV data with use of the MAR intervention, we found that 4 of the 7 participants with adequate NIV adherence at 7-days were using the MAR intervention. Of the remaining three participants who successfully transitioned to NIV, two didn't feel the need to use the music and one was in the SC group.

Changes in anxiety and quality of life

The outcomes for anxiety (HADS) and quality of life (AQoL-8D) are presented in Table 2. As stated previously, we did not plan to conduct comparisons between the groups due to the non-randomised nature of the trial design.

Table 2. T-tests results for comparison of baseline with immediately subsequent timepoint for the entire cohort expressed as mean (standard deviation).

Outcome measure	Baseline	7-day	3-month	P value
Anxiety (HADS n=11)	5.6 (3.3)	4.4 (2.2)	*	0.190
Quality of Life (AQoL-8D, n=9)	64.0 (16.7)		67.7 (12.4)	0.441

Abbreviations: HADS, Hospital Anxiety and Depression Scale; AQoL-8D, Assessment of Quality of Life. Higher scores equate to poorer outcome for both HADS and AQoL.
** 3-month HADS data was only available for 8 participants. Results of the ANOVA analysis of the three HADS timepoints is presented in the text below.*

The mean anxiety scores on the HADS showed a decrease in anxiety of 1.2 points from baseline to 7-day review that was not statistically significant (p=.19, Table 2). The minimally important difference on the HADS is 1.5 points[49]. For the 8 participants with 3-month HADS data there was a mean decrease in anxiety of 1.6 points from baseline to 3-month follow-up. A repeated measures analysis of variance for anxiety found no significant effects (p=.213).

There was minimal change in quality of life as measured by the AQoL-8D (mean increase of 3.7 points, representing a

decrease in HRQoL) from baseline to 3-month follow-up (p=.441, Table 2).

Research Question 3 - What is the experience of people with MND using MAR during transition to NIV?

9 participants (8 MAR, 1 SC) were interviewed at 7-days post NIV implementation. The results of this analysis are published in detail elsewhere [50], but a brief summary is presented here. A total of 27 themes were derived from a phenomenological analysis [51]. There were no common themes (across all 9 participants). 13 significant themes (greater than 3 participants), and 14 individual themes (2 or less participants) were further distilled down into six Global Meaning Units: 1) the transition to using NIV is fraught with challenges, 2) NIV can positively impact quality of life, 3) the transition to using NIV was smooth, 4) the relaxing and distracting effects of the MAR were useful in this context, 5) once starting NIV, MAR was deemed either unnecessary or not useful, and 6) individualization of MAR program and equipment was important. The 6 Global Meaning Units were grouped together to create the following Distilled Essence:

For these individuals with MND using a music-assisted relaxation intervention during the transition to NIV, NIV was thought to have a positive impact on quality of life. For some, the transition to using NIV was smooth, while for others it was fraught with challenges. Some participants found the relaxing and distracting effects of the MAR useful in this context while others found that once they started NIV, MAR was deemed unnecessary (n=1), not useful (n=1), or was difficult to incorporate due to MND-associated cognitive decline (n=1). All participants considered that the individualization of the MAR program and equipment was an important consideration in using the music intervention successfully.

Research Question 4 -What are the challenges to conducting research in the MND population?

Participant recruitment, uptake, retention and completion rates were low. Several factors led to implementation difficulties. Referral to NIV assessment may be a distressing time for some participants. For some, the prospect of needing NIV assistance with breathing comes not long after receiving the diagnosis of this terminal disease and for others is associated with significant deterioration towards its terminal nature. The additional invitation to participate in research at this time was clearly too much for some of these people. Further, 17 participants were not able to complete both the initial assessment and MAR training session within 7 days of attending the assessment session. This was an often-unavoidable consequence of the short timeframe between the researchers being notified that a potential participant was being assessed for NIV and the NIV implementation session. Approximately one-third of potential participants were never invited to the project for this reason.

Discussion

Feasibility of the study design

The difficulty with recruiting participants was often related to timing. The short time between assessment for NIV and implementation was an issue for some, and for others it was too overwhelming to try two new interventions (MAR and NIV) at the same time. Both of these issues could potentially be addressed by introducing the MAR intervention earlier in the disease progression, prior to NIV assessment and implementation.

Just under half (18 of 42) of invited participants consented to participate in the study and 15 of these (83%) chose the music assisted relaxation (MAR) intervention. It was not possible to determine any characteristics differentiating between the participants who chose MAR or SC, because of low numbers in the SC cohort. The interesting point here is that the majority of consenting participants wanted to try the music intervention, which may suggest high acceptability of a MAR intervention if it was available.

There were limitations to not using random allocation, as we could not have equal numbers in the two conditions for statistical analyses or predictor modeling. The attrition rate was high (50%); many people became too unwell to complete the study and two died. Therefore, in spite of the apparent demand for the intervention, future research implemented with this population will require much larger sample sizes to account for the high attrition rate.

Limited efficacy

Our qualitative data revealed that some participants found that the MAR intervention provided beneficial relaxing and distracting effects that assisted their NIV transition process, while others found it unnecessary or not useful once they started NIV. It was difficult to derive a pattern of NIV use and MAR use due to individual variations and small sample size. It is interesting to note that of the 6 MAR participants that successfully transitioned to NIV, 4 used the music intervention and 2 did not. There was only one SC participant with NIV usage data and this participant also achieved adequate NIV adherence at 7 days.

Feasibility of the intervention protocol

The intervention protocol was successfully implemented with the majority of MAR participants. There were some technical issues with setting up music access for some participants and also difficulty fitting the music therapy assessment and production of the MAR CDs/playlists in between recruitment

and NIV implementation at times. The majority of participants who selected the MAR condition received the intervention positively, suggesting good acceptability. For those participants who did not use the MAR intervention, this was primarily due to logistical/technical issues to do with accessing the music or feeling too overwhelmed with NIV implementation to try something new. The logistical issues included: lack of time between recruitment and NIV implementation, difficulty setting up a CD player at bedside, difficulty using a CD player, difficulty setting up music playlists on personal music listening devices, including copyright, and technical difficulties with syncing. For several participants there was too little time between recruitment and NIV implementation to conduct the music therapy assessment and produce the MAR CDs. The previous suggestion to introduce the MAR intervention earlier in the disease progression would also address this intervention timing issue. Participant preferences for how to access their music also need to be taken into account and any logistical issues addressed. This includes an assessment of functional ability (ie. can the participant start/stop the music independently), technical knowledge, and access to resources (ie. what kind of equipment do they prefer/are familiar with and can use).

Suitability of the assessment measures

Although the NIV usage data was routinely collected from each participant's machine, there were several practicality issues that led to missing data, including equipment breakdown/ replacement and blank/broken SD memory cards. However, we found that all six participants who achieved adequate adherence at 7 days had maintained adequate adherence at 3 months. Regardless of MAR use, our results have provided preliminary data indicating the importance of supporting people to achieve adequate NIV usage within the first 7 days in order to attain adequate ongoing NIV usage.

The HADS tool may not have been the best choice of measure for anxiety in this population as it is designed to measure clinical anxiety, rather than the situational and reactive anxiety that commonly occur in people with MND transitioning to NIV. Further, there was a possible ceiling effect for this tool as only two participants were classified with mild anxiety and one with moderate anxiety according to their baseline HADS scores. This may indicate that people were rating their anxiety lower than it was. O'Callaghan [52] discussed a similar tendency for cancer patients to respond to studies in a positively biased manner due to trying to please the researcher, to behave in a way they perceived as socially desirable, and/or to fight disease mindset. Interestingly, the qualitative data provided different information about participants' perceived level of anxiety. In spite of low anxiety scores on the HADS, many participants reported feeling anxious about commencing NIV. To our knowledge the AQoL-8D had not been used in MND research previously and thus we cannot be sure that it was sensitive enough to measure change in this study. Despite the slight (non-significant) mean decrease in health-related quality of life measured by the AQoL-8D, the qualitative results suggested that NIV was perceived to have a positive impact on quality of life. The divergence of results from both quantitative measures with the qualitative findings support the need for mixed methods research to explore these outcomes using a variety of data types. It was not possible to determine the AQoL-8D's sensitivity to change in this study due to the small overall sample size and lack of numbers in the SC group. However, we found no obvious reasons to suggest that this measure was not appropriate for a study such as this, apart from issues related to declining cognitive capacity discussed in the following section.

Practicality issues impacting data collection and missing data

Due to the medical fragility of this population, many of the self-report measures (HADS and AQoL-8D) were missing, particularly at the 3-month time point when declining health precluded many participants from completing the self-report measures. A limitation of the study design is that we did not exclude or screen for cognitive impairments despite fronto-temporal dementia being highly prevalent in MND [53]. The survey results for some participants therefore may have been influenced by cognitive decline. Further, proxy completion of questionnaires was necessary at times and may have affected the results, particularly for the 3-month data when disease progression was more severe.

Adaptation and integration

Although MAR interventions have been used previously with similar populations (e.g. mechanically ventilated patients), the lack of a comparison group in this study meant that we were unable to determine the extent to which outcomes of MAR intervention are similar or different between NIV and mechanically ventilated populations. The MAR intervention was feasible in terms of integration into the current model of healthcare delivery. Education sessions with healthcare staff are now routinely conducted to encourage early referrals of patients with MND for music therapy assessment.

Conclusion

This research has contributed important findings regarding the feasibility of delivering and examining the effects of MAR on transition to NIV for people with MND. In the small sample tested, we found some demand for and acceptability of a music-based intervention in this setting. There were obvious

technical and logistical issues that need to be taken into account regarding timely and accessible provision of a MAR intervention within the treatment trajectory of NIV implementation. In addition, careful consideration should be given to the choice of outcome measures to ensure that these will be sensitive enough to measure change. Although recruitment rates were low and attrition was high, this feasibility study has demonstrated that the delivery of a MAR intervention is practicable and points to the need for future studies in this area to be more highly powered.

Our preliminary results have indicated that all participants who met the criteria for adequate NIV use at 7 days (at least 4 hours per night for at least 5 days per week) continued to meet these criteria at 3 months. Therefore, any intervention that can assist people to adequately transition to NIV use in the first 7 days of use may be of long-term benefit. Conflicting results from quantitative measures and qualitative data for our secondary outcomes (anxiety and quality of life) support the need for mixed method research in this area.

Referral for NIV assessment caused anxiety for many participants according to the qualitative data. Further, there is often only a short time window between NIV assessment and implementation. By introducing the MAR assessment and training earlier in the MND disease trajectory, it is possible that more patients may be willing and able to effectively use this intervention to assist their NIV transition process. The earlier introduction of MAR may also assist with recruitment for future studies in this area.

References

1. Jackson CE, Lovitt S, Gowda N, Anderson F, Miller RG. Factors correlated with NPPV use in ALS. Amyotroph Lateral Scler. 2006. 7(2): p. 80-85.
2. Talbot K, Marsden R. Facts: Motor Neuron Disease. Oxford: Oxford University Press; 2008.
3. Kleopa KA, Sherman M, Neal B, Romano GJ, Heiman-Patterson T. Bipap improves survival and rate of pulmonary function decline in patients with ALS. J Neurol Sci. 1999. 164(1): p. 82-88.
4. Berlowitz DJ, Howard M, Fiore J, et al. Identifying who will benefit from Non-Invasive Ventilation in Amyotrophic Lateral Sclerosis/Motor Neurone Disease in a clinical cohort. Journal of Neurology, Neurosurgery, and Psychiatry. 2015. 87(3) doi: 10.1136/jnnp-2014-310055. [Epub ahead of print].
5. Bourke SC, Gibson GJ. Non-invasive ventilation in ALS: current practice and future role. ALS and Other Motor Neuron Disorders. 2004. 5: p. 67-71.
6. Sundling IM, Ekman SL, Weinberg J, Klefbeck B. Patients' with ALS and caregivers' experiences of non-invasive home ventilation. Adv Physiother. 2009. 11(3): p. 114-120.
7. Bourke SC, Bullock RE, Williams TL, Shaw PJ, Gibson GJ. Noninvasive ventilation in ALS Indications and effect on quality of life. Neurology. 2003. 61(2): p. 171-177.
8. Newsom-Davis IC, Lyall RA, Leigh PN, Moxham J, Goldstein LH. The effect of non-invasive positive pressure ventilation (NIPPV) on cognitive function in amyotrophic lateral sclerosis (ALS): a prospective study. J Neurol Neurosurg Psychiatry. 2011. 71: p. 482–487.
9. Radunovic A, Annane D, Rafiq MK, N. M. Mechanical ventilation for amyotrophic lateral sclerosis/motor neuron disease. Cochrane Database of Systematic Reviews 2013. Issue 3. Art. No.: CD004427. DOI: 10.1002/14651858.CD004427.pub3.
10. Rafiq MK, Proctor AR, McDermott CJ, Shaw PJ. Respiratory management of motor neurone disease: a review of current practice and new developments. Pract Neurol. 2012. 12(3): p. 166-176.
11. Foley G, Timonen V, Hardiman O. Experience of services as a key outcome in amyotrophic lateral sclerosis (ALS) care: the case for a better understanding of patient experiences. American Journal of Hospice and Palliative Medicine. 2011. 29(5): p. 362–367.
12. Cazzolli PA, Oppenheimer EA. Home mechanical ventilation for amyotrophic lateral sclerosis: nasal compared to tracheostomy-intermittent positive pressure ventilation. J Neurol Sci. 1996. 139: p. 123-128.
13. Kaub-Wittemer D, von Steinbüchel N, Wasner M, Laier-Groeneveld G, Borasio GD. Quality of life and psychosocial issues in ventilated patients with amyotrophic lateral sclerosis and their caregivers. J Pain Symptom Manage. 2003. 26(4): p. 890-896.
14. Torheim H, Gjengedal E. How to cope with the mask? Experiences of mask treatment in patients with acute chronic obstructive pulmonary disease-exacerbations. Scand J Caring Sci. 2010. 24(3): p. 499-506.
15. Seighalani MZ, Ghahari S, Zarbakhsh M. The effectiveness of music therapy on depression, anxiety and self-esteem of patients with multiple sclerosis. Advances in Environmental Biology. 2014. 20: p. 253-261.
16. Bradt J, Dileo C, Shim M. Music interventions for preoperative anxiety. Cochrane Database of Systematic Reviews. 2013. Issue 6. Art. No.: CD006908. DOI: 10.1002/14651858.CD006908.pub2.
17. Tan X, Yowler CJ, Super DM, Fratianne RB. The efficacy of music therapy protocols for decreasing pain, anxiety, and muscle tension levels during burn dressing changes: a prospective randomized crossover trial. Journal of Burn Care & Research. 2010. 31(4): p. 590-597.
18. Lai HL, Hwang ML, Chen CJ, Chang KF, Peng TC, Chang FM. Randomised controlled trial of music on state anxiety and physiological indices in patients undergoing root canal treatment. J Clin Nurs. 2008. 17(19): p. 2654-2660.
19. Beaulieu-Boire G, Bourque S, Chagnon F, Chouinard L, Gallo-Payet N, Lesur O. Music and biological stress dampening in mechanically-ventilated patients at the intensive care unit ward: A prospective interventional randomized crossover trial. J Crit Care. 2013. 28(4): p. 442-450.
20. Chlan LL, Weinert CR, Heiderscheit A, et al. Effects of patient-directed music intervention on anxiety and sedative exposure in critically ill patients receiving mechanical ventilatory support: a randomized clinical trial. J Am Med Assoc. 2013. 309(22): p. 2335-2344.
21. Han L, Li J, Sit J, Chung L, Jiao Z, Ma W. Effects of music intervention on physiological stress response and anxiety level of mechanically ventilated patients in China: a randomised controlled trial. J Clin Nurs. 2010. 18: p. 978-987.
22. Hunter B, Oliva R, Sahler O, Gaisser D, Salipante D, Arezina C. Music therapy as a adjunctive treatment in the management of stress for patients being weaned from mechanical ventilation. J Music Ther. 2010. 47(3): p. 198-219.
23. Korhan E, Khorshid L, Uyar M. The effect of music therapy on physiological signs of anxiety in patients receiving mechanical ventilatory support. ournal of Clinical Nursing. 2011. 20: p. 1026-1034.
24. Lee O, Chung Y, Chan M, Chan W. Music and its effect on the physiological responses and anxiety levels of patients receiving mechanical ventilation: a pilot study. J Clin Nurs. 2005. 14: p. 609-620.
25. Bradt J, Dileo C. Music interventions for mechanically ventilated patients. Cochrane Database of Systematic Reviews 2014. Issue 12. Art. No.: CD006902. DOI: 10.1002/14651858.CD006902.pub3. .
26. Phillips SD, *The effect of music entrainment on respiration of patients on mechanical ventilation in the intensive care unit*. 2007, Florida State University: Florida.

27. Maranto C. Applications of music in medicine. in: Music Therapy in Health and Education, M. Heal and T. Wigram, Editors. London. Jessica Kingsley Publishers: 1993, p. 153-174.
28. Thaut M, Davis W. The influence of subject selected versus experimenter-chosen music on affect, anxiety, and relaxation. J Music Ther. 1993. 30(4): p. 210-223.
29. Chlan LL. Effectiveness of a music therapy intervention on relaxation and anxiety for patients receiving ventilator assistance. Heart Lung. 1998. 27(3): p. 169–176.
30. Lee DW, Chan KW, Poon CM, et al. Relaxation music decreases the dose of patient-controlled sedation during colonoscopy: a prospective randomized controlled trial. Gastrointest Endosc. 2002. 55: p. 33-36.
31. Harikumar R, Raj M, Paul A, et al. Listening to music decreases need for sedative medication during colonoscopy: a randomized, controlled trial. Indian J Gastroenterol. 2006. 25(1): p. 3.
32. Lepage C, Drolet P, irard M, Grenier Y, DeGagné R. Music decreases sedative requirements during spinal anesthesia. Anesth Analg. 2001. 93(4): p. 912-916.
33. Ayoub CM, Rizk LB, Yaacoub CI, Gaal D, Kain ZN. Music and ambient operating room noise in patients undergoing spinal anesthesia. Anesth Analg. 2005(100): p. 5.
34. LaGasse AB. Pilot and feasibility studies: application in music therapy research. J Music Ther. 2013. 50(4): p. 304-320.
35. Bowen DJ, Kreuter M, Spring B, et al. How we design feasibility studies. American Journal of Preventative Medicine. 2009. 36(5): p. 452-457.
36. Krout RE. Music listening to facilitate relaxation and promote wellness: Integrated aspects of our neurophysiological responses to music. The Arts in Psychotherapy. 2007. 34: p. 134-131.
37. Schneck DJ, Berger DS. The music effect: Music physiology and clinical applications. London and Philadelphia: Jessica Kingsley Publishers.; 2006.
38. Heiderscheit A, Madson A. Use of the iso principle as a central method in mood management: A music psychotherapy clinical case study. Music Therapy Perspectives 2015. 33(1): p. 45-52.
39. Nickol AH, Hart N, Hopkinson NS, Moxham J, Simonds A, Polkey MI. Mechanisms of improvement of respiratory failure in patients with restrictive thoracic disease treated with non-invasive ventilation. Thorax. 2005. 60(9): p. 754-760.
40. Sawyer A, Gooneratne N, Marcus C, Ofer D, Richards K, Weaver T. A systematic review of CPAP adherence across age groups: Clinical and empiric insights for developing CPAP adherence interventions. Sleep Med Rev. 2011. 15(6): p. 343-356.
41. Hawthorne G. Assessing utility where short measures are required: Development of the Short Assessment of Quality of Life-8 (AQoL-8) instrument. Value Health. 2009. 12(6): p. 448-957.
42. Richardson J, Elsworth G, Iezzi A, et al. Increasing the sensitivity of the AQoL inventory for the evaluation of interventions affecting mental health. Melbourne Australia: Centre for Health Economics Monash University. 2011.
43. Richardson J, Iezzi A. Psychometric validity and the AQoL 8D Multi attribute utility instrument. Melbourne Australia: Centre for Health Economics Monash University. 2011. 13.
44. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatria Scandinavia. 1983. 67(6): p. 361-370.
45. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression scale. An updated literature review. J Psychosom Res. 2002. 52: p. 69–77.
46. Horne-Thompson A, Bolger K. An investigation comparing the effectiveness of a live music therapy session and recorded music in reducing anxiety for patients with amyotrophic lateral sclerosis/motor neurone disease. Australian Journal of Music Therapy. 2010. 21: p. 23-38.
47. Cedarbaum JM, Stambler N, Malta E, et al. The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. J Neurol Sci. 1999. 169(1): p. 13-21.
48. Castrillo-Viguera C, Grasso DL, Simpson E, Shefner J, Cudkowicz ME. Clinical significance in the change of decline in ALSFRS-R. Amyotroph Lateral Scler. 2010. 11(1-2): p. 178-180.
49. Puhan MA, Frey M, Büchi S, Schünemann HJ. The minimal important difference of the hospital anxiety and depression scale in patients with chronic obstructive pulmonary disease. Health and Quality of Life Outcomes. 2008. 6(46): p. 1-6.
50. Davies, R., Tamplin, J., Baker, F.A., Bajo, E., Bolger, K., Sheers, N. & Berlowitz, D.J. (2016). Music-assisted relaxation during transition to non-invasive ventilation in people with motor neuron disease: A qualitative case series. British Journal of Music Therapy. 30(2), 74-82. doi: 10.1177/1359457516669153.
51. McFerran K, Grocke D. Understanding music therapy experiences through interviewing: A phenomenological microanalysis. in: Microanalysis in music therapy: Methods, techniques and applications for clinicians, researchers, educators and students T. Wosch and T. Wigram, Editors. Philadelphia, PA. Jessica Kingsley Publishers: 2007, p. 273-284.
52. O'Callaghan C. Bringing music to life: A study of music therapy and palliative care experiences in a cancer hospital. J Palliat Care. 2001. 17(3): p. 155-160.
53. Kiernan MC, Vucic S, Cheah BC, et al. Amyotrophic lateral sclerosis. Lancet. 2011. 377: p. 942-955.

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Appendix 1 - Playlists

	Celtic	
Song Title	**Recording artist/ composer**	**Album**
Simple relaxation introduction	Eleanor Bajo	
Sigma	Irish national chamber choir/ John Tate/ Rhonan Surgrue/ secret garden	Dreamcatcher (2001)
Song from a secret garden	David Agnew, John Tate, secret garden	Secret Garden (1996)
Passacaglia	John Tate, secret garden, Simon Elmes	Dreamcatcher (2001
I know a rose tree	Secret Garden, Anuna	Superstar Christmas (2014)
In our tears	Anuna, John Tate, Secret Garden	Dreamcatcher (2001)
Hymn to hope	Davy Spillane, Rolf Lovland, Secret Garden	White Stones (1997)

	Classical 1	
Song Title	**Recording artist/ composer**	**Album**
Simple relaxation introduction	Eleanor Bajo	
Romance (The Gadfly)	Dmitri Shostakovich	Most relaxing classical album in the world…ever ! vol 2 disc 1.
Fantasia on Greensleeves	Various	Relaxing Adagios Disc 1
Nocturne No. 2 in E Flat Op. 9 No. 2	Fryderyk Chopin	Most relaxing classical album in the world…ever ! vol 2 disc 1.
Traumerei	Robert Schumann	Most relaxing classical album in the world…ever ! vol 2 disc 1.
Schindler's List Theme	New World Philharmonic	Most relaxing classical album in the world…ever ! vol 2 disc 1.
Miserere Mei, Deus (Extract)	Gerald Finley/ Stephen Cleobury	Most relaxing classical album in the world…ever ! vol 2 disc 1.

Classical 2		
Song Title	**Recording artist/ composer**	**Album**
Simple relaxation introduction	Eleanor Bajo	
Orfeo ed Euridice, opera, Wq 41: Dance of the blessed spirits.	Various	Night music II
Puccini: Madama Butterfly – humming chorus	Various	Relaxing Adagios Disc 2
Gymnopedie No. 3	Various	Relaxing Adagios Disc 1
One hand, one heart	Various	Swooning
Pieces (8) for piano, Op. 76: No. 3, Intermezzo	Various	Night music II
Aritz Adarean	Various	Relaxing Adagios Disc 1
JS Bach: Suite No. 3 in D, BWV 1068 Air	Various	Relaxing Adagios Disc 1
Carmen Suite No. 1	Various	Relaxing Adagios Disc 1
String Quintet, D956	Various	Relaxing Adagios Disc 1

Nature		
Song Title	**Recording artist/ composer**	**Album**
Simple relaxation introduction	Eleanor Bajo	
Castle of Dreams	Tony O'Connor, Paul Clement	Summer Rain
Dreams	Tony O'Connor, Paul Clement	Summer Rain
Raindancing	Tony O'Connor, Paul Clement	Summer Rain
Fairy Tale	Tony O'Connor, Paul Clement	Summer Rain
Dew	Tony O'Connor, Paul Clement	Summer Rain

Popular		
Song Title	**Recording artist/ composer**	**Album**
Simple relaxation introduction	Eleanor Bajo	
Eternal Flame	Various	The ultimate moods collection
Three times a lady	Various	The ultimate moods collection
Without you	Various	The ultimate moods collection
Woman	Various	The ultimate moods collection, Disc 3
Wonderful Tonight	Various	The ultimate moods collection, Disc 3
Always on my mind	Various	The ultimate moods collection, Disc 3
She	Various	The ultimate moods collection, Disc 3