Clinical effectiveness of music interventions for dementia and depression in older people (MIDDEL): a multinational, cluster-randomised controlled trial

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Summary

Background Dementia and depression are among the leading causes of global disease burden. Effective and scalable interventions are needed to address the effect of these conditions, and music interventions are a promising non-pharmacological approach. The aim of this study was to determine the effectiveness of music interventions on depressive symptoms among care home residents with dementia in Australia, Germany, the Netherlands, Norway, Türkiye, and the UK.

Methods Music Interventions for Dementia and Depression in Elderly care was a large, multinational, cluster-randomised controlled trial with a 2×2 factorial design to examine the effects of group music therapy, recreational choir singing, or both compared with standard care. The trial was done in 86 care home units across Australia, Germany, the Netherlands, Norway, Türkiye, and the UK. Care home units were required to host at least ten residents who met the inclusion criteria. Participants were required to be aged 65 years or older; a full-time resident in a participating care home unit; have dementia as indicated by a Clinical Dementia Rating score of 0·5–3 and a Mini-Mental State Examination score of 26 or less; have mild depressive symptoms as indicated by a Montgomery–Åsberg Depression Rating Scale (MADRS) score of at least 8; and a clinical diagnosis of dementia. Care home units with residents with dementia and depressive symptoms were randomly assigned (1:1:1:1; block randomisation stratified by site, using a computer-generated list) to group music therapy, recreational choir singing, a combination of these strategies, or standard care. The primary outcome was MADRS assessed at 6 months in the intention-to-treat population, which included all participants with available data. Assessors were masked but care staff, intervention providers, and residents were not masked due to the nature of the intervention. Intervention effects were analysed with ANCOVA for the total sample and per country. The trial was registered at ClinicalTrials.gov, NCT03496675, and is completed.

Findings Between July 18, 2018, and Feb 1, 2023, 86 care home units with 1021 residents were enrolled and randomly assigned to one of the four groups. 22 care home units with 258 residents were randomly assigned to group music therapy, 22 care home units with 281 residents were allocated to recreational choir singing, 21 care home units with 244 residents were assigned to a combination of both group music therapy and recreational choir singing, and 21 care home units with 238 residents were assigned to standard care. The mean age of residents was 85·6 years (SD 7·4); most residents (747 [73·2%]) were female and 274 (26·8%) were male. Intention-to-treat analysis of 751 residents with data at 6 months showed no significant effect on MADRS scores of either recreational choir singing versus no recreational choir singing (β 0·4 [95% CI −1·3 to 2·1]; p=0·68), group music therapy versus no group music therapy (β 0·8 [−1·0 to 2·6]; p=0·37), or the interaction between recreational choir singing and group music therapy (β −0·6 [−3·1 to 1·9], p=0·63; β represents mean difference estimated from ANCOVA). Effects varied between countries. No related adverse events were reported and acute medical hospital admission rates were similar across groups at 3 months and 6 months.

Interpretation Internationally, active group music interventions as conducted in this study do not reduce depressive symptoms more than standard care in the long term. Country was the strongest predictor for differences in effects, underlining the importance of cultural and systemic differences. Intervention guidelines and health-care policies need to be carefully tailored to the specific contexts of care home populations and levels of care. Future multisite trials should focus on more narrowly defined target groups or contexts to reduce the risk of heterogeneity overshadowing potential effects of interventions. Although music interventions might be beneficial for people with dementia, there is a need to harmonise their implementation and investigate the mechanisms through which they work.

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Introduction

Dementia and depression are among the leading causes of global disease burden and are projected to rise in the coming decades.[1] They frequently co-occur in the older population (aged 65 years and older), complicating diagnosis and treatment and exacerbating cognitive and functional decline. Effective and scalable interventions are needed to alleviate symptoms and improve wellbeing among people living with dementia and address the substantial effect on health-care systems, caregivers, and communities.

Because of the known limitations of pharmacological treatment, developing and evaluating non-pharmacological interventions is very important.[2,3] Music interventions have emerged as a promising non-pharmacological approach, leveraging the emotion and memory-evoking properties of

Research in context

Evidence before this study

The previous evidence base for music-based therapeutic interventions for people living with dementia, summarised in a 2018 Cochrane review by van der Steen and colleagues, showed that music interventions have the potential to reduce depressive symptoms in this population. The overall quality of the evidence for end-of-treatment effects was moderate (11 studies, 503 participants). For long-term effects, defined as at least 4 weeks after end of treatment (six studies, 354 participants), there was low-quality evidence of no reduction. An update conducted during the present study (van der Steen and colleagues 2025; searches until 2023) showed an increase in the number of studies, but similar conclusions, although the Australian data from the present study were included. More recently, in January, 2025, we searched PubMed with no language restrictions for randomised controlled trials published between July 1, 2017, and Jan 9, 2025, using the string "dementia OR Alzheimer(s) AND depress* AND music therapy OR music intervention", filtered for population age: 65 years and older. The search identified three additional studies which measured the effect of active group music interventions on depressive symptoms in people living with dementia. Sample sizes in the three studies ranged from 42 to 121 and only included participants with mild-to-moderate cognitive impairment. One of the studies investigated a 12-week group music intervention, with weekly 120-min singing sessions delivered by a professional choir conductor accompanied by a psychologist. The study found no significant effects on depressive symptoms using the Geriatric Depression Scale. The second and third studies investigated music therapy led by certified music therapists, using the Cornell Scale for Depression in Dementia. The second study provided group music therapy in 60-min sessions delivered twice per week for 6 weeks. There was a significant reduction in depressive symptoms compared with the control group, and effects were sustained at the 3-month follow-up. The third study provided individual music therapy in 45-min sessions delivered once weekly for 16 weeks and found a significant reduction in depressive symptoms from pre-intervention to post-intervention compared with the control group. The low-to-moderate quality of evidence and lack of studies on long-term outcomes corroborates the need for well-conducted large-scale randomised controlled trials to better understand the clinical effects of specific music-based interventions on depression for people living with dementia.

Added value of this study

To our knowledge, Music Interventions for Dementia and Depression in Elderly (MIDDEL) is the largest trial of music interventions in dementia care to date. The interventions, group music therapy and recreational choir singing, were conducted in a more intensive and standardised manner than that of previous trials. The sample of participants was large compared with in previous studies and covered different health systems. In the overall sample, no effects of music interventions conducted for 6 months were found on the main outcome of depressive symptoms, or on secondary outcomes of cognitive impairment, neuropsychiatric symptoms, quality of life, and care staff burden. Subgroup analyses showed that the interventions had positive effects on depressive symptoms at 3 months among those who attended at least 50% of the maximum number of sessions, and among those with moderate-to-severe dementia. Contrasting effects across the six participating countries suggest important differences related to cultural contexts, national residential care admission policies, levels of baseline care, and local implementation of interventions.

Implications of all the available evidence

The findings of MIDDEL indicate that across countries, group music therapy and recreational choir singing do not result in consistent improvement of depressive symptoms among care home residents with dementia in the long term. Effects seem to depend on the cultural and systemic context in which interventions are implemented, as well as on quality-controlled implementation of the interventions themselves. Interventions as currently implemented across countries might be effective in the shorter term and for subgroups with moderate to severe levels of dementia. Intervention guidelines and health-care policies for people living with dementia need to be carefully tailored to the specific contexts of care home populations and levels of care. Future multisite studies should focus on more narrowly defined target groups or contexts to reduce the risk of heterogeneity in effects across health systems; harmonise implementation of interventions; and examine links between mechanisms, direct goals, and downstream effects.

music.[4] Music interventions involve emotional, cognitive, social, and biological mechanisms interacting in dynamic ways.[5] Musical memory is partly independent from other memory systems and often preserved in Alzheimer's disease.[6] Music interventions can be delivered in individual, group, and community settings, either as a targeted clinical intervention by trained music therapists, or as a broader recreational activity by other music professionals, or formal or informal carers. Music interventions have shown the potential to reduce depressive symptoms, anxiety, and overall behavioural problems, and to improve emotional wellbeing and quality of life among people living with dementia.[2] However, existing evidence is generally of low-to-medium quality and there is a need for well-conducted, large-scale randomised controlled trials to better understand these effects.[2]

The Music Interventions for Dementia and Depression in Elderly care (MIDDEL) trial examined two distinct types of music interventions for people living with dementia and depressive symptoms in care homes across five European countries and Australia.[5] Specifically, we selected group music therapy and recreational choir singing, which had previously shown differential effects in a smaller cluster-randomised trial.[7] Both use active music-making but differ in types of music (playing *vs* singing), group size, and necessary qualifications of the intervention provider.[5,7] Replicating and expanding the previous trial, MIDDEL aimed to determine the effectiveness of group music therapy and recreational choir singing—both separately and in combination—on depressive symptoms and other outcomes, and to examine heterogeneity of treatment effects across subgroups. Here, we report on the primary outcome of depression symptoms at 6 months, and other continuous outcomes measured within the same time frame.

Methods

Study design

MIDDEL was a large, multinational, cluster-randomised controlled trial, which used a 2×2 factorial design to examine the effects of group music therapy, recreational choir singing, and these two therapies combined (compared with standard care alone) on depressive symptoms in care home residents with dementia and depressive symptoms. The trial was conducted in 86 care home units across Australia, Germany, the Netherlands, Norway, Türkiye, and the UK. Care home units were required to host at least ten residents who met the inclusion criteria.

Ethical approvals were obtained from the relevant institutional human research ethics committees in each country (appendix p 2). The Australian part of the project attained funding first and started recruitment in 2018,[8] while the five European countries started recruitment in 2021. Recruitment was completed in 2023. Due to delays related to funding and COVID-19 among the European countries, the results from the Australian part of the trial have previously been published.[8] This decision was endorsed by the Data and Safety Monitoring Committee based on the earlier completion date in Australia. The current paper includes the data from the total sample in all six countries.

The trial was registered at clinicaltrials.gov (NCT03496675) and is completed. A published protocol and statistical analysis plan are available online.[5] The following amendments were made after the publication of the protocol, but before Australian outcomes were known: inclusion criteria were expanded to a Clinical Dementia Rating (CDR) score of 0·5–3 (very mild to severe; from 0·5–2) to include a broader spectrum of people living with dementia; CDR was excluded as a secondary outcome at follow-up due to burden on participants and limited expectations for change; the Severe Impairment Battery (SIB-8) was added as a secondary outcome measure of cognitive impairment in Europe as it was considered more sensitive to changes in cognition over time; and the list of participating countries was updated based on funding acquisition.

Participants

Eligibility was defined on two levels: care home units, and individual residents. A care home unit was defined as the smallest organisational unit within a site (a care home or residential care facility) where residents lived and were cared for together by staff (eg, a community or floor within a larger care home). Participating care home units were those expected to have at least ten eligible and consenting residents and that were not providing music-based interventions as part of usual care at the time of enrolment.

Inclusion criteria for residents were: age 65 years or older; full-time resident in a participating care home unit; dementia as indicated by a CDR score of 0·5–3 and a Mini-Mental State Examination (MMSE) score of 26 or less; mild depressive symptoms as indicated by a Montgomery-Åsberg Depression Rating Scale (MADRS) score of at least 8; a clinical diagnosis of dementia according to ICD-10 research criteria (not consistently available in the UK);[9] and written informed consent provided by the resident or by proxy from a legal representative in cases where participants were unable to consent themselves. Data on sex were collected by care home staff based on available records at the home (male or female). Data on race or ethnicity were not collected.

Eligible care home units were identified by the research teams in each country, in collaboration with local service providers. All potentially eligible residents at participating units were screened by assessors (members of the research team or health care professionals collaborating in the project), and informed consent (self or proxy) was obtained before completing the full baseline assessment.

Care staff, employed for at least 0·4 full-time equivalent at the time the unit was randomised, were also recruited to assess the secondary outcome of staff burden.

See Online for appendix

Randomisation and masking

Care home units were allocated (1:1:1:1) to group music therapy, recreational choir singing, group music therapy and recreational choir singing, or standard care. Block

randomisation (block size of four) was used to ensure that each site would have a balanced distribution between the interventions. Randomisation of care home units was performed by author CG at NORCE using a computer-generated randomisation list (separate list for each country, produced in R), after baseline assessments had been completed and entered into the electronic database. For cases in which it was possible, four units were randomised at a time to ensure allocation concealment.

Due to the nature of the interventions, care staff, intervention providers, and residents were not masked to the intervention provided. Assessors performing data collection were masked to intervention allocation; this was achieved by relying on assessors who did not normally work in the same unit. Success of masking was determined by asking assessors whether they had inadvertently become aware of the allocation at each follow-up assessment. In total, one case of unmasking was reported at 3 months, and the assessor was replaced to ensure masking for the remaining assessments. No cases of unmasking were reported at 6 months.

Procedures

All care home units continued with standard care as locally available. In units allocated to a music intervention, the intervention was provided in 45-min sessions twice weekly during month 1–3 (frequency and duration as in the previous trials[5,7]), and once weekly during months 4–6 (extension not included in previous trials). Continuation of interventions was allowed after this period, depending on local availability. In line with usual practice[5] and a consensus developed for the present trial,[10] group music therapy was conducted in small, closed groups of about five participants, while recreational choir singing was conducted in larger groups of about ten participants and could also be attended by residents not participating in the project. Manuals for both interventions were developed, and interventionists received two online training sessions consisting of general training (project information, documentation, problem-solving scenarios, supervision, and self-assessment) and intervention-specific training based on the content of the manuals (appendix pp 43–46). Intervention sessions were video-recorded, and researchers and interventionists met regularly for supervision and self-assessment. Number of sessions provided and residents' attendance was recorded by the interventionists.

Group music therapy was provided by trained music therapists, registered with the appropriate professional association or registration body in their country. Before sessions commenced, music therapists collected information about residents' background (familial, cultural, musical) from family and care staff and offered each participant an initial 20-min assessment to determine music preferences and establish rapport. Each 45-min group music therapy session included: (1) an opening with a welcome song and introductions; (2) song singing, reminiscence, and discussion; optional elements of (3) improvisation using musical instruments and (4) movement to music; (5) continuation of element 2 (song singing, reminiscence, and discussion); and (6) a closing with a goodbye song and farewell. The core principle of group music therapy is to affect regulation through active, reciprocal music-making, facilitating relationships between therapist and participants, and between residents within the group.[5] Group music therapy aimed to meet the psychosocial needs of each individual resident and work in the here and now by acknowledging and responding to participants' immediate emotional expressions and incorporating them into meaningful musical expressions for therapeutic gain.[11,12]

Recreational choir singing was provided by skilled musicians with choir leading skills. Each 45-min choir singing session included: (1) an introduction with a welcome song, recap of previous session, or current events; (2) physical and vocal warm-up and exercises; (3) familiar song singing; (4) learning new songs or harmony parts to familiar songs; and (5) a goodbye song and farewell. Music varied between repertoires and seasonal and circumstantial factors. Sessions focused on providing a familiar musical environment for participants through a creative and recreational, but also relatively structured process. Recreational choir singing involves a combination of cognitive, physical, and psychosocial engagement components,[13] aimed to promote social interaction, connectedness, emotional well-being, and enjoyment of music-making in a group. Biographically and culturally grounded resources for the group were used to stimulate shared positive associations. For participants who had engaged in music activities in the past, the intervention could also enable continuation of the familiar social experience of music-making in everyday life.

For the combined group, participants engaged in both group music therapy and choir singing, alternatingly (on different days of the week). The standard care group comprised the usual care and activities available at the care home, which could range from provision of medications to various social activities.

Data collection was completed using paper forms in the local language. Care staff responded to items regarding demographics and service use on behalf of residents, and mode of assessment (self, proxy, or both) for clinical measures was based on residents' ability to respond and guidebook recommendations for the individual instruments. Forms were consecutively entered into an electronic database (OpenClinica for Australian data; REDCap for European data), after which paper forms were stored or destroyed according to the data security requirements of each participating institution.

Measures assessed at baseline only, as part of the inclusion criteria, were CDR, a semi-structured interview that rates level of dementia as 0 (normal), 0·5 (very mild or questionable), 1 (mild), 2 (moderate), or 3 (severe);[14] and the MMSE, assessing cognitive function with a sumscore ranging 0–30, where 26 or less indicates cognitive impairment.[15]

Outcomes

Outcomes were assessed at baseline and at month 3 and 6 after randomisation. The primary outcome timepoint was 6 months, based on the duration of the interventions and life expectancy in residential care. Long-term follow-up at 12 months after randomisation was conducted where this was possible within the project period and results will be published separately.

The primary outcome was depressive symptoms at 6 months using the MADRS, a ten-item scale with items ranging from 0 (no abnormality) to 6 (severe).[16] The total sumscore ranged from 0 to 60, with higher scores indicating higher severity of depressive symptoms. Cutoffs for mild (<20) versus moderate or severe (≥20) symptoms were used for subgroup analyses.[17]

Secondary outcomes were cognitive impairment, assessed using the eight-item SIB-8, a brief screening tool with a total sumscore ranging 0–16, with higher scores indicating less impairment;[18] neuropsychiatric symptoms using the Neuropsychiatric Inventory Questionnaire (NPI-Q), including 12 items assessing symptom severity (ranging 0–36) and associated distress on caregivers (ranging 0–60), with higher scores indicating higher severity or distress;[19] generic quality of life using the EQ Visual Analogue Scale (EQ-VAS), a visual analogue scale indicating today's health from 0 (worst health you can imagine) to 100 (best health you can imagine);[20] and disease-specific quality of life using the Quality of Life in Alzheimer's Dementia (QOL-AD), a 13-item scale with a total sumscore ranging 13–52, with higher scores indicating a higher quality of life.[21] For care home staff, we measured staff burden using the Professional Care Team Burden Scale (PCTB), a ten-item self-assessment scale with a total sumscore ranging 0–40, with higher scores indicating a higher burden.[22] Measures of costs, quality-adjusted life-years, psychotropic drug use, biomarkers, and sick leave days among care staff were also assessed at follow-up and will be reported elsewhere.

Regarding the assessment of safety and adverse events, a Data and Safety Monitoring Committee with unmasked access to the data received and reviewed updates on hospital admissions and all-cause mortality (time to death) biannually throughout the project period. When the COVID-19 pandemic occurred, this was expanded with information about numbers of residents and staff infected and restrictions introduced at each care home unit (complete lockdown; no access for assessors, interventionists, or visitors; and any other preventive measures).

Statistical analysis

The trial was powered to detect small-to-medium effects (d=0·33, based on a previous trial;[7] range 0·20–0·50) on the primary outcome (depression symptoms; main effects: group music therapy *vs* no group music therapy [recreational choir group and standard care group]; recreational choir singing *vs* no recreational choir singing [group music therapy and standard care group]; Bonferroni-adjusted to two-sided 2·5%; adjusted for cluster size ten with intraclass correlation coefficient 0·01–0·10[5]). Statistical analyses followed the statistical analysis plan published with the protocol.[5] We used descriptive methods to characterise the sample by group. Baseline characteristics of participants lost to follow-up at 6 months and those who were still participating were compared using tests for independent samples (*t*-test, χ^2-test). Intervention effects were analysed using the intention-to-treat approach, using all available outcome data. Effects of each intervention on continuous outcomes at 6 months were assessed using linear mixed-effects models. Based on new insights,[23] we replaced longitudinal multivariate linear mixed-effects models[5] with ANCOVA linear mixed-effects models (regression of the outcome at 6 months on the interventions, adjusted for the outcome at baseline, with random intercept for care home unit; estimating and comparing single models for each intervention and full models for both interventions and their interaction). Additionally, we estimated a longitudinal linear mixed-effects model for each outcome variable at baseline (to account for baseline differences between groups), 3 months, and 6 months depending on timepoint, intervention, and their interaction, with random intercept per participant, care home unit, and country. Adjusting for baseline in this way is equivalent to analysing change from baseline but avoids the disadvantages of using change scores (regression to the mean, bias).[23] We repeated both the ANCOVA and the longitudinal linear mixed-effects models for the per-protocol-sample (≥50% of maximum preplanned sessions attended) for the sensitivity analysis. In addition to analyses for all participants from all countries, we conducted the same analyses stratified per country. The ANCOVA for the primary outcome (MADRS) was repeated for several subgroups (with *vs* without COVID-19 lockdown; mild [CDR <2] *vs* moderate or severe dementia [CDR ≥2]; mild [MADRS <20] *vs* moderate or severe depressive symptoms [MADRS ≥20]; sex; and country). We did not use multiple imputation because it does not improve estimations when outcomes are missing, and missingness of explanatory variables was negligible. The general significance level was set to 0·05. In all models β denotes the coefficients (ie, the model adjusted mean differences) and is presented with 95% CIs. Due to the two comparisons (group music therapy *vs* no group music therapy and recreational choir singing *vs* no recreational choir singing) we used Bonferroni adjustment, leading to a marginal significance level of 0·025. Safety events were reported descriptively. The analyses were done using R 4.4.1 and the graphics were created using Matlab 9.14 (R2023b).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between July 18, 2018, and Feb 1, 2023, 116 care home units in 64 care homes were assessed for eligibility. 30 care home

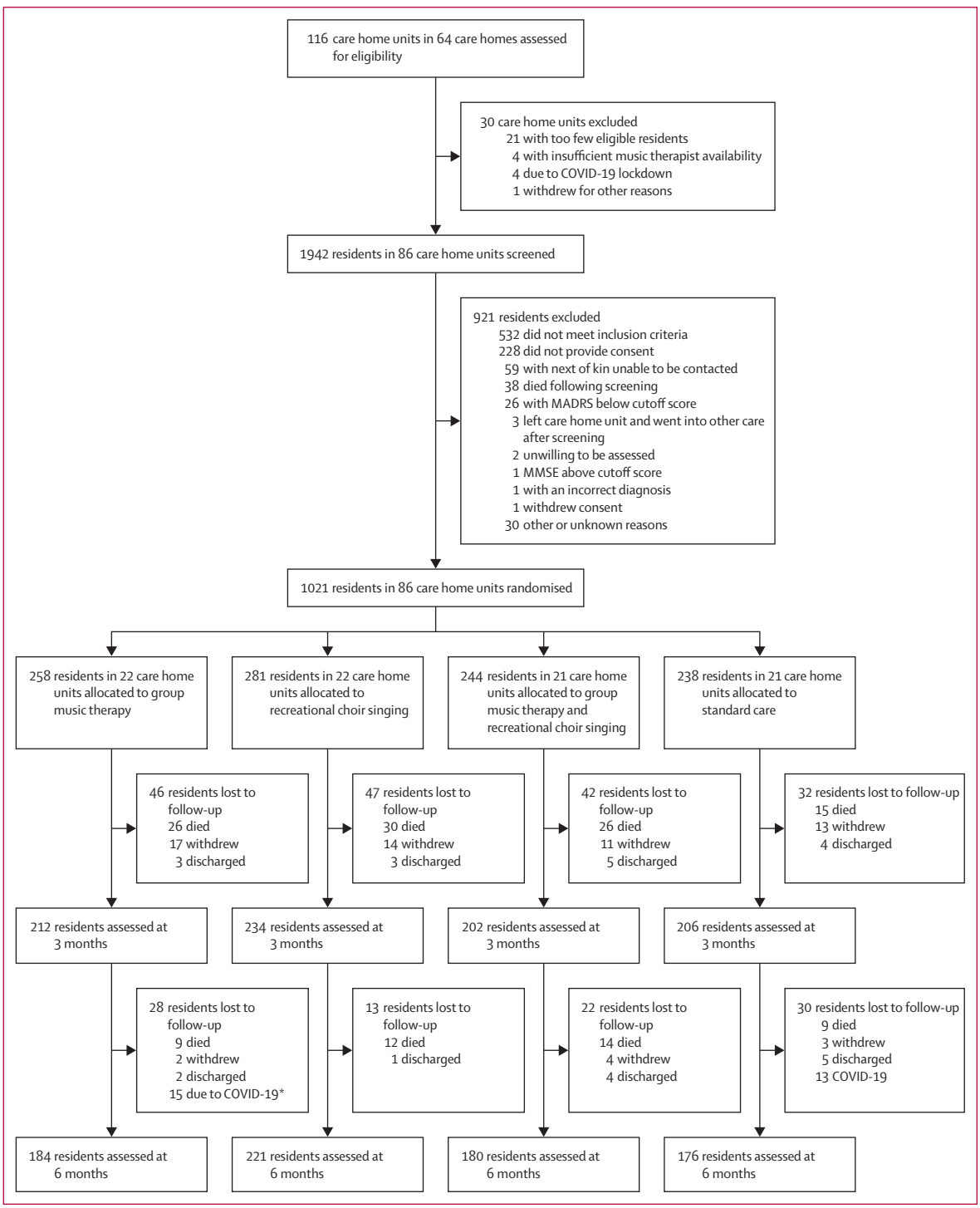

Figure 1: **Trial profile**
MADRS=Montgomery-Åsberg Depression Rating Scale. MMSE=Mini-Mental State Examination. *Due to COVID-19 outbreak or lockdown at the care home unit.

units were excluded, and 1942 residents in 86 care home units were screened for study inclusion. 921 residents were excluded (mainly due to non-fulfilment of inclusion criteria or lack of informed consent), and 86 care home units with 1021 enrolled residents were randomly assigned to one of the four groups. 22 care home units with 258 residents were randomly assigned to group music therapy, 22 care home units with 281 residents were allocated to recreational choir

	Total sample (n=86 care home units; n=1021 residents)	Group music therapy (n=22 care home units; n=258 residents)	Recreational choir singing (n=22 care home units; n=281 residents)	Group music therapy and recreational choir singing (n=21 care home units; n=244 residents)	Standard care (n=21 care home units; n=238 residents)
Age (years)	85·6 (7·4)	85·5 (7·6)	85·3 (7·6)	85·4 (7·4)	86·1 (6·8)
Sex					
Female	747 (73·2%)	189 (73·3%)	205 (73·0%)	183 (75%)	170 (71·4%)
Male	274 (26·8%)	69 (26·7%)	76 (27·0%)	61 (25%)	68 (28·6%)
Marital status					
Married	257/1000 (25·7%)	58/255 (22·7%)	77/274 (28·1%)	69/238 (29%)	53/233 (22·7%)
Single, unmarried, separated, or divorced	156/1000 (15·6%)	36/255 (14·1%)	42/274 (15·3%)	44/238 (18·5%)	34/233 (14·6%)
Widow or widower	556/1000 (55·6%)	157/255 (61·6%)	143/274 (52·2%)	119/238 (50·0%)	137/233 (58·8%)
Not known	31/1000 (3·1%)	4/255 (1·6%)	12/274 (4·4%)	6/238 (2·5%)	9/233 (3·9%)
Education level					
Primary education or less	223/849 (26·3%)	49/218 (22·5%)	70/230 (30·4%)	51/204 (25·0%)	53/197 (26·9%)
Secondary education	355/849 (41·8%)	102/218 (46·8%)	85/230 (37%)	93/204 (45·6%)	75/197 (38·1%)
Tertiary or further education	138/849 (16·3%)	32/218 (14·7%)	42/230 (18·3%)	31/204 (15·2%)	33/197 (16·8%)
Other general education	10/849 (1·2%)	4/218 (1·8%)	2/230 (0·9%)	2/204 (1·0%)	2/197 (1·0%)
Not known	123/849 (14·5%)	31/218 (14·2%)	31/230 (13·5%)	27/204 (13·2%)	34/197 (17·3%)
Diagnosis					
Dementia in Alzheimer's disease (F00 + G30)	298/987 (30·2%)	87/251 (34·7%)	76/274 (27·7%)	70/237 (29·5%)	65/225 (28·9%)
Vascular dementia (F01)	76/987 (7·7%)	18/251 (7·2%)	22/274 (8·0%)	18/237 (7·6%)	18/225 (8·0%)
Dementia in diseases classified elsewhere (F02)	18/987 (1·8%)	3/251 (1·2%)	6/274 (2·2%)	3/237 (1·3%)	6/225 (2·7%)
Unspecified dementia (F03)	432/987 (43·8%)	102/251 (40·6%)	124/274 (45·3%)	113/237 (47·7%)	93/225 (41·3%)
Frontotemporal dementia (G31·0)	8/987 (0·8%)	0	1/274 (0·4%)	5/237 (2·1%)	2/225 (0·9%)
Dementia with Lewy bodies (G31·83)	16/987 (1·6%)	2/251 (0·8%)	4/274 (1·5%)	3/237 (1·3%)	7/225 (3·1%)
Other dementia or not known	139/987 (14·1%)	39/251 (15·5%)	41/274 (15·0%)	25/237 (10·5%)	34/225 (15·1%)
MMSE (0–30)*	9 (7·3)	8·9 (7·2)	8·8 (7·2)	9·1 (7·2)	9·3 (7·4)
CDR (0·5–3)†	2·2 (0·8)	2·1 (0·8)	2·3 (0·8)	2·2 (0·7)	2·1 (0·8)
CDR 0·5 (very mild or questionable dementia)	32/1015 (3·2%)	10/258 (3·9%)	6/276 (2·2%)	5/243 (2·1%)	11/238 (4·6%)
CDR 1 (mild dementia)	170/1015 (16·7%)	48/258 (18·6%)	44/276 (15·9%)	37/243 (15·2%)	41/238 (17·2%)
CDR 2 (moderate dementia)	403/1015 (39·7%)	103/258 (39·9%)	98/276 (35·5%)	102/243 (42·0%)	100/238 (42%)
CDR 3 (severe dementia)	410/1015 (40·4%)	97/258 (37·6%)	128/276 (46·4%)	99/243 (40·7%)	86/238 (36·1%)
MADRS (0–60)‡	19·3 (8·1)	18·4 (8·3)	19·9 (8·1)	19·3 (7·7)	19·4 (8·3)
MADRS respondent					
Self	75/1007 (7·4%)	32/254 (12·6%)	24/280 (8·6%)	7/239 (2·9%)	12/234 (5·1%)
Proxy	922/1007 (91·6%)	222/254 (87·4%)	256/280 (91·4%)	227/239 (95·0%)	217/234 (92·7%)
Both	10/1007 (1·0%)	0	0	5/239 (2·1%)	5/234 (2·1%)
SIB-8§	8·3 (5·4)	8·4 (5·3)	8·1 (5·6)	9·1 (5·2)	7·7 (5.3)
NPI-Q–severity (0–36)¶	10 (6·7)	9·8 (6·9)	10·1 (6·9)	10·4 (6·8)	9·6 (6·1)
NPI-Q–caregiver distress (0–60)‖	10·3 (10·3)	10·2 (10·6)	10·5 (11·1)	11·2 (10·3)	9·4 (8·9)
EQ-VAS (0–100)**	58·7 (20·6)	61·6 (19·8)	55·3 (21·2)	59·3 (18·4)	59 (22·4)
EQ-VAS respondent					
Self	208/1009 (20·6%)	61/257 (23·7%)	53/276 (19·2%)	53/241 (22·0%)	41/235 (17·4%)
Proxy	724/1009 (71·8%)	180/257 (70%)	209/276 (75·7%)	164/241 (68·0%)	171/235 (72·8%)
Both	77/1009 (7·6%)	16/257 (6·2%)	14/276 (5·1%)	24/241 (10·0%)	23/235 (9·8%)
QoL-AD (0–39)††	16·4 (9·5)	16·7 (9·1)	15·6 (9·3)	16·5 (9·7)	17·1 (9·9)

(Table 1 continues on next page)

singing, 21 care home units with 244 residents were assigned to a combination of both group music therapy and recreational choir singing, and 21 care home units with 238 residents were assigned to standard care. No care home units dropped out during the study. Of the 1021 residents enrolled within the 86 care home units, 761 (74·5%) remained at the 6-month follow-up (figure 1). A total of 549 care staff at the care home units completed the PCTB at baseline, and 398 (72·5%) remained at 6 months (appendix p 36). Main reasons for dropout of residents were death (n=141), withdrawal (n=64), discharge from the care home (n=27), and COVID-19 lockdowns (n=28; figure 1). Residents who dropped out were more commonly male, had lower cognitive ability, lower generic quality of life,

	Total sample (n=86 care home units; n=1021 residents)	Group music therapy (n=22 care home units; n=258 residents)	Recreational choir singing (n=22 care home units; n=281 residents)	Group music therapy and recreational choir singing (n=21 care home units; n=244 residents)	Standard care (n=21 care home units; n=238 residents)
(Continued from previous page)					
QoL-AD respondent					
Self	474/1008 (47·0%)	127/256 (49·6%)	102/279 (36·6%)	125/237 (52·7%)	120/236 (50·8%)
Proxy	504/1008 (50·0%)	129/256 (50·4%)	164/279 (58·8%)	103/237 (43·5%)	108/236 (45·8%)
Both	30/1008 (3·0%)	0	13/279 (4·7%)	9/237 (3·8%)	8/236 (3·4%)
PCTB (0–40)‡‡	8·9 (3·7)	8·9 (3·7)	8·6 (3·7)	8·8 (3·9)	9·3 (3·5)

Data are mean (SD) or n/N (%). *MMSE data are from 1015 residents in the total sample: 258 in the group music therapy group, 279 in the recreational choir singing group, 243 in the combined group, and 235 in the standard care group. †CDR data are from 1015 residents in the total sample: 258 in the group music therapy group, 276 in the recreational choir singing group, 243 in the combined group, and 238 in the standard care group. ‡MADRS data are from 1009 residents in the total sample: 257 in the group music therapy group, 277 in the recreational choir singing group, 244 in the combined group, and 231 in the standard care group. §SIB-8 data are from 688 residents in the total sample: 178 in the group music therapy group, 195 in the recreational choir singing group, 159 in the combined group, and 156 in the standard care group (SIB-8 data were not collected in Australia). ¶NPI-Q severity data are from 1008 residents in the total sample: 257 in the group music therapy group, 278 in the recreational choir singing group, 238 in the combined group, and 235 in the standard care group. ||NPI-Q caregiver distress data are from 1009 residents in the total sample: 257 in the group music therapy group, 278 in the recreational choir singing group, 238 in the combined group, and 236 in the standard care group. **EQ-VAS data are from 913 residents in the total sample: 225 in the group music therapy group, 239 in the recreational choir singing group, 224 in the combined group, and 225 in the standard care group. ††QoL-AD data are from 1013 residents in the total sample: 258 in the group music therapy group, 279 in the recreational choir singing group, 240 in the combined group, and 236 in the standard care group. ‡‡PCTB data are from 434 residents in the total sample: 108 in the group music therapy group, 108 in the recreational choir singing group, 111 in the combined group, and 107 in the standard care group. MMSE=Mini-Mental State Examination. CDR=Clinical Dementia Rating. MADRS=Montgomery-Åsberg Depression Rating Scale. SIB=Severe Impairment Battery. NPI-Q=Neuropsychiatric Inventory-Questionnaire. EQ-VAS=EuroQol Visual Analogue Scale. QoL-AD=Quality of Life in Alzheimer's Disease. PCTB=Professional Care Team Burden Scale.

Table 1: **Baseline characteristics**

more severe dementia, and more depressive symptoms (appendix p 9).

The mean age of residents was 85·6 years (SD 7·4) and the majority (747 [73·2%]) were female and 274 (26·8%) were male (table 1). Most participants had a moderate (403 [39·7%] of 1015) or severe (410 [40·4%] of 1015) clinical dementia rating, and were diagnosed with either unspecified dementia (432 [43·8%] of 987) or Alzheimer's disease dementia (298 [30·2%] of 987). Data on race or ethnicity were not collected. Session attendance varied due to participants' health and scheduling issues (appendix p 10). Very few cases of treatment contamination were usually due to residents being transferred to another unit (participants attending recreational choir singing while initially living in a unit randomly assigned to group music therapy; appendix p 10). No residents in the standard care group attended any group music therapy or recreational choir singing sessions.

The primary outcome of MADRS for the total intention-to-treat sample decreased for all interventions and the standard care group between baseline and 3 months and remained relatively stable at 6 months (figure 2). We did not observe significant differences between the interventions: combining all countries, the ANCOVA models (reporting full models; similar results in single models) had no p values lower than p=0·37 (table 2). The small non-significant effects on MADRS in the intention-to-treat analysis across countries (recreational choir singing: 0·4 [95% CI –1·3 to 2·1]; group music therapy: 0·8 [–1·0 to 2·6]; interaction: –0·6 [–3·1 to 1·9]; table 2) correspond to negligible effect sizes (Cohen's d $\leq$0·1; table 2). Neither the per-protocol analysis nor longitudinal models (linear mixed-effects models, not reported here but available upon request) changed these results (appendix p 23). The individual countries showed varying patterns (figure 2); this high heterogeneity is also reflected in the high intraclass correlation coefficient (table 2). Recreational choir singing had a significantly unfavourable effect on MADRS in the Netherlands (β 5·4 [95% CI 1·7 to 9·1]; p=0·0049) and in the UK (β 6·0 [2·1 to 9·9]; p=0·0027), while there was a beneficial effect of recreational choir singing on MADRS in Norway (β –5·3 [–9·9 to –0·8]; p=0·023) and Türkiye (β –12·0 [–20·8 to –3·1]; p=0·0098; appendix pp 11–22). The remaining countries did not show any clear pattern. We did not observe an effect of group music therapy or the combination of both interventions (interaction) compared with the absence of that intervention. Note that there were few observations for some of the countries (Türkiye) and there appeared to be some differences between the interventions at baseline (Norway). Per-protocol analyses for the individual countries showed a beneficial effect of recreational choir singing in Australia, Norway, and Türkiye, and an unfavourable effect of recreational choir singing in the UK, while there were no significant effects in Germany and the Netherlands (appendix pp 25–35).

The ANCOVA for secondary outcomes (table 2; figure 3) showed that there were no significant effects for either SIB-8, NPI symptom severity, NPI caregiver distress, EQ-VAS, or QOL-AD. For PCTB, the ANCOVA confirmed that recreational choir singing had an unfavourable effect (β 1·3 [95% CI 0 to 2·5]; p=0·046), and the interaction between recreational choir singing and group music therapy showed a beneficial effect (β –2 [–3·7 to –0·2]; p=0·028).

Figures visualising secondary outcomes for each country and the results of ANCOVA are shown in the appendix (appendix pp 11–22, 37–42). Australia showed an unfavourable effect of recreational singing on PCTB. The Netherlands

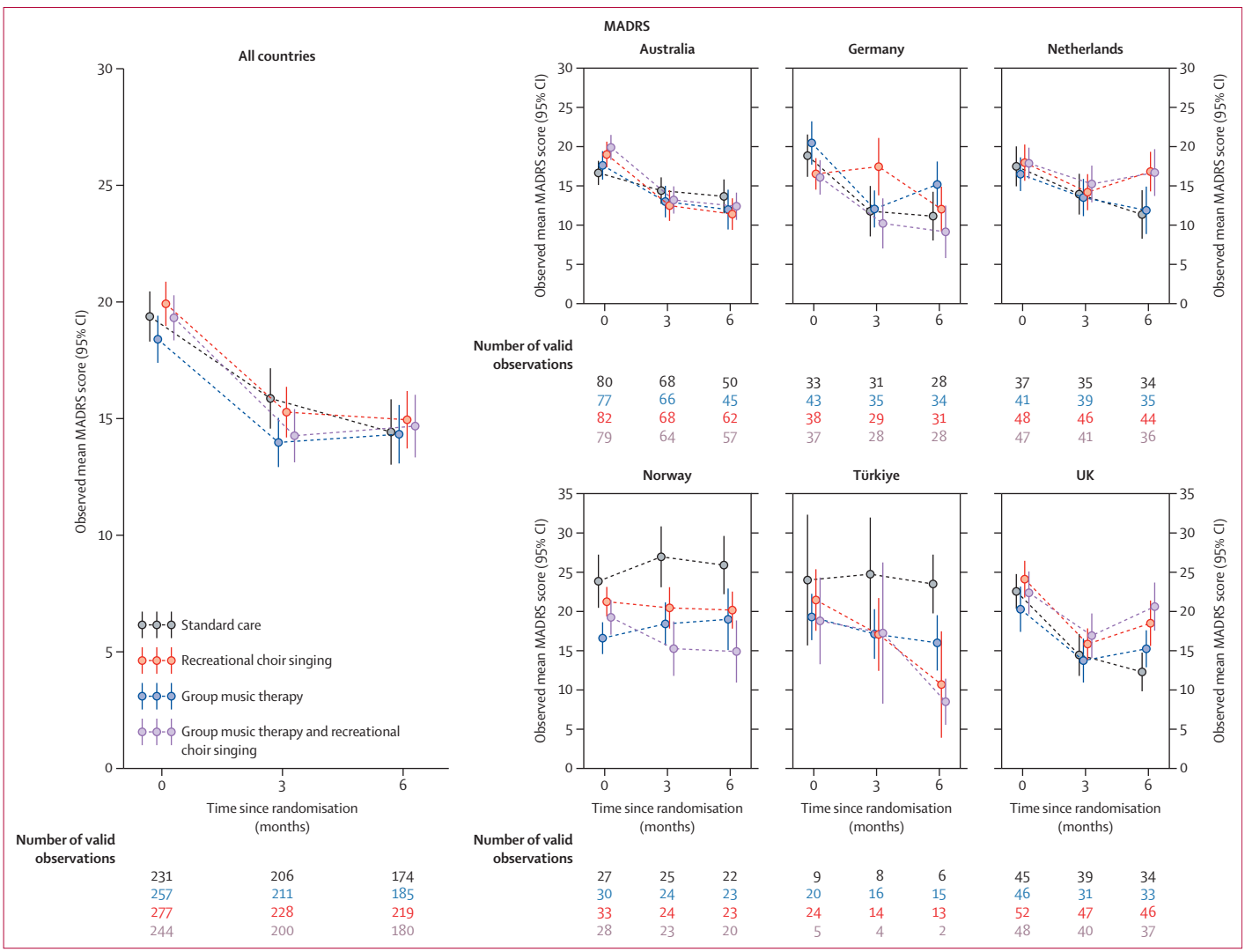

Figure 2: **Primary outcome data of depressive symptoms over 6 months**
Data are observed means and 95% CIs of MADRS for all participants with valid data at 0, 3, and 6 months from randomisation. MADRS=Montgomery-Åsberg Depression Rating Scale.

showed an unfavourable effect of group music therapy on SIB-8. Norway showed an unfavourable effect of recreational choir singing on NPI caregiver distress, while group music therapy showed a beneficial effect on NPI caregiver distress. Türkiye showed beneficial effects of group music therapy on NPI symptom severity. The UK showed unfavourable effects of recreational choir singing on NPI symptom severity and EQ-VAS, but a beneficial effect of recreational choir singing on QOL-AD; while group music therapy showed a beneficial effect on QOL-AD. Furthermore, in the UK, there was an unfavourable interaction effect of recreational choir singing with group music therapy compared with the main (additive) effects of both interventions combined on NPI caregiver distress and QOL-AD, but a beneficial interaction effect of the combination on EQ-VAS. Per-protocol analyses for all outcomes are reported in the appendix (pp 23–35).

No adverse events related to the trial procedures were reported. Acute medical hospital admission rates were similar across groups (3 months: 18 participants in the group music therapy group, 27 participants in the recreational choir singing group, 12 participants in the combined group, and 15 participants in the standard care group; 6 months: 12 participants in the group music therapy group, 20 participants in the recreational choir singing group, nine participants in the combined group, and ten participants in the standard care group).

Sensitivity and subgroup analyses suggested positive intervention effects in the per-protocol sample at 3 months (p=0·0004) but not at 6 months (figure 4). Inconsistent effects were observed in those affected by lockdowns along with more positive effects among residents with moderate or severe dementia at 3 months (p=0·011); however, effects varied across countries.

	Marginal estimates			ANCOVA		
	Number of residents	Mean (95% CI)	Mean difference (95% CI)	β (95% CI)	p value	Cohen's d (95% CI)
All countries: MADRS (N=751, ICC=0·315)						
Standard care	170	14·2 (12·9 to 15·5)	..	0 (ref)	..	..
Recreational choir singing	184	14·5 (13·4 to 15·7)	0·4 (–0·8 to 1·6)	..	..	..
Group music therapy	217	15 (13·7 to 16·2)	0·8 (–0·4 to 2·1)	..	..	..
Group music therapy and recreational choir singing	180	14·7 (13·5 to 16)	0·6 (–0·7 to 1·8)	..	..	..
All recreational choir singing*	364	14·6 (13 to 13)	0 (–2·4 to 2·5)	0·4 (–1·3 to 2·1)	0·68	0 (–0·1 to 0·2)
All group music therapy†	397	14·9 (13·1 to 13·1)	0·5 (–1·9 to 3)	0·8 (–1·0 to 2·6)	0·37	0·1 (–0·1 to 0·2)
Interaction recreational choir singing × group music therapy	..	..	..	–0·6 (–3·1 to 1·9)	0·63	0 (–0·2 to 0·1)
All countries: SIB-8 (N=751, ICC=0·222)						
Standard care	170	9·4 (8·8 to 10·1)	..	0 (ref)	..	..
Recreational choir singing	184	8·6 (8·0 to 9·2)	–0·8 (–1·5 to –0·2)	..	..	..
Group music therapy	217	8·9 (8·3 to 9·6)	–0·5 (–1·1 to 0·1)	..	..	..
Group music therapy and recreational choir singing	180	8·7 (8·1 to 9·4)	–0·7 (–1·4 to 0)	..	..	..
All recreational choir singing*	364	8·7 (7·8 to 7·8)	–0·5 (–1·8 to 0·8)	–0·8 (–1·7 to 0)	0·062	–0·2 (–0·3 to 0)
All group music therapy†	397	8·8 (7·9 to 7·9)	–0·2 (–1·4 to 1·1)	–0·5 (–1·4 to 0·4)	0·27	–0·1 (–0·3 to 0·1)
Interaction recreational choir singing × group music therapy	..	..	..	0·6 (–0·6 to 1·9)	0·32	0·1 (–0·1 to 0·3)
All countries: NPI–symptom severity (N=751, ICC=0·292)						
Standard care	170	7·7 (6·9 to 8·6)	..	0 (ref)	..	..
Recreational choir singing	184	8·4 (7·7 to 9·2)	0·7 (–0·1 to 1·5)	..	..	..
Group music therapy	217	7·8 (6·9 to 8·6)	0 (–0·8 to 0·9)	..	..	..
Group music therapy and recreational choir singing	180	8·4 (7·5 to 9·2)	0·6 (–0·2 to 1·5)	..	..	..
All recreational choir singing*	364	8·4 (7·3 to 7·3)	0·6 (–1·0 to 2·3)	0·7 (–0·4 to 1·8)	0·23	0·1 (–0·1 to 0·2)
All group music therapy†	397	8·0 (6·9 to 6·9)	–0·1 (–1·7 to 1·6)	0 (–1·1 to 1·2)	0·96	0 (–0·1 to 0·1)
Interaction recreational choir singing × group music therapy	..	..	..	–0·1 (–1·7 to 1·5)	0·92	0 (–0·2 to 0·1)
All countries: NPI–caregiver distress (N=751, ICC=0·277)						
Standard care	170	7·1 (6·0 to 8·1)	..	0 (ref)	..	..
Recreational choir singing	184	8·1 (7·2 to 9·1)	1·1 (0·1 to 2·1)	..	..	..
Group music therapy	217	6·3 (5·3 to 7·3)	–0·8 (–1·8 to 0·3)	..	..	..
Group music therapy and recreational choir singing	180	8·7 (7·6 to 9·7)	1·6 (0·5 to 2·7)	..	..	..
All recreational choir singing*	364	8·4 (7·0 to 7·0)	1·8 (–0·3 to 3·8)	1·1 (–0·4 to 2·5)	0·14	0·1 (0 to 0·3)
All group music therapy†	397	7·4 (5·9 to 5·9)	–0·2 (–2·3 to 1·8)	–0·8 (–2·3 to 0·7)	0·31	–0·1 (–0·2 to 0·1)
Interaction recreational choir singing × group music therapy	..	..	..	1·3 (–0·8 to 3·4)	0·21	0·1 (–0·1 to 0·2)
All countries: EQ-VAS (N=751, ICC=0·255)						
Standard care	170	61·6 (58·8 to 64·4)	..	0 (ref)	..	..
Recreational choir singing	184	61·5 (58·9 to 64·1)	–0·1 (–2·8 to 2·6)	..	..	..
Group music therapy	217	63·9 (61·1 to 66·8)	2·3 (–0·5 to 5·2)	..	..	..
Group music therapy and recreational choir singing	180	62·5 (59·6 to 65·3)	0·9 (–2·0 to 3·7)	..	..	..
All recreational choir singing*	364	62 (58·1 to 58·1)	-0·9 (–6·5 to 4·6)	–0·1 (–4·0 to 3·7)	0·95	0 (–0·2 to 0·1)
All group music therapy†	397	63·3 (59·2 to 59·2)	1·7 (–3·8 to 7·3)	2·3 (–1·7 to 6·3)	0·26	0·1 (–0·1 to 0·2)
Interaction recreational choir singing × group music therapy	..	..	..	–1·4 (–6·9 to 4·2)	0·63	0 (–0·2 to 0·1)
All countries: QOL-AD (N=751, ICC=0·209)						
Standard care	170	15·4 (14·3 to 16·5)	..	0 (ref)	..	..
Recreational choir singing	184	15·5 (14·5 to 16·5)	0·1 (–0·9 to 1·2)	..	..	..
Group music therapy	217	14·7 (13·7 to 15·8)	–0·6 (–1·7 to 0·4)	..	..	..
Group music therapy and recreational choir singing	180	13·3 (12·2 to 14·4)	–2·0 (–3·1 to –0·9)	..	..	..
All recreational choir singing*	364	14·4 (13·0 to 13·0)	–0·6 (–2·7 to 1·6)	0·1 (–1·4 to 1·6)	0·86	0 (–0·1 to 0·2)
All group music therapy†	397	14·1 (12·6 to 12·6)	–1·3 (–3·5 to 0·8)	–0·6 (–2·2 to 0·9)	0·42	–0·1 (–0·2 to 0·1)
Interaction recreational choir singing × group music therapy	..	..	..	–1·5 (–3·7 to 0·6)	0·16	–0·1 (–0·2 to 0)

(Table 2 continues on next page)

Discussion

MIDDEL was a large cluster-randomised controlled trial examining the effects of two different music interventions for care home residents with dementia and depressive symptoms across six countries. Main findings showed no clinically relevant effects of either intervention on the outcomes investigated in the total sample, including depressive symptoms, cognitive impairment, neuropsychiatric symptoms, quality of life, and increased care staff burden. Findings of no beneficial effects are similar to previous

	Marginal estimates			ANCOVA		
	Number of residents	Mean (95% CI)	Mean difference (95% CI)	β (95% CI)	p value	Cohen's d (95% CI)
(Continued from previous page)						
All countries: PCTB (N=751, ICC=0·213)						
Standard care	170	8·3 (7·4 to 9·1)	..	0 (ref)	..	..
Recreational choir singing	184	9·5 (8·6 to 10·4)	1·3 (0·4 to 2·1)	..	..	..
Group music therapy	217	9·1 (8·2 to 10)	0·9 (0 to 1·7)	..	..	..
Group music therapy and recreational choir singing	180	8·4 (7·5 to 9·3)	0·1 (–0·7 to 1)	..	..	..
All recreational choir singing*	364	9 (7·7 to 7·7)	0·2 (–1·5 to 2)	1·3 (0 to 2·5)	0·046	0·3 (0 to 0·5)
All group music therapy†	397	8·8 (7·5 to 7·5)	–0·1 (–1·9 to 1·6)	0·9 (–0·4 to 2·1)	0·18	0·2 (–0·1 to 0·4)
Interaction recreational choir singing × group music therapy	..	..	..	–2·0 (–3·7 to –0·2)	0·028	–0·3 (–0·5 to 0)

*All recreational choir singing: only recreational choir singing and recreational choir singing and group music therapy (vs only group music therapy and standard care). †All group music therapy: only group music therapy and recreational choir singing and group music therapy (vs only recreational choir singing and standard care). ANCOVA with site as random intercept. MADRS=Montgomery-Åsberg Depression Rating Scale. ICC=intraclass correlation coefficient. SIB=Severe Impairment Battery. NPI=Neuropsychiatric Inventory. EQ-VAS=EuroQol Visual Analogue Scale. QoL-AD=Quality of Life in Alzheimer's Disease. PCTB=Professional Care Team Burden Scale.

Table 2: **6-month outcomes for all countries combined in the intention-to-treat population**

multinational trials of music interventions,[24,25] but contrast with local studies, including the Australian MIDDEL cohort[8] and the German MIDDEL predecessor,[7] and with systematic reviews suggesting benefits of music interventions for depressive symptoms, behavioural problems, emotional wellbeing, and quality of life, but little or no effect on cognition.[2,3] More generally, interventions including exercise, social interaction, and cognitive stimulation (all of which are elements of group music therapy and recreational choir singing[5,8]) reduce depression symptoms in people with dementia.[26]

MIDDEL was conducted across socioeconomically and culturally diverse countries with vastly different social and health-care systems. The heterogeneity across countries might have overshadowed potential benefits of the interventions and is reflected in higher ICCs (0·315 for the primary outcome, in contrast to 0·01 to 0·10 assumed in the sample size calculation) and reduced power. National differences in admission policies, participants' baseline characteristics and levels of baseline care, cultural differences, and differences in the implementation of interventions might all have contributed to this variability. Recreational choir singing showed particularly high heterogeneity: it appeared beneficial in some countries (Australia, Norway, and Türkiye) and ineffective or harmful in others (Germany, the Netherlands, and the UK). Unfavourable effects on care staff burden seen across countries appeared to be driven primarily by two countries (Australia and the UK). This might indicate differences in the quality of intervention provision. There is little regulation of recreational choir singing training or provision internationally. For example, in Türkiye, neither psychosocial interventions nor musical activities are currently part of standard care, and MIDDEL was first to apply standardised musical interventions regularly in this context. Additionally, baseline depressive symptoms were high in the Türkish sample.[27] Both music interventions complied with recommendations of cultural adaption for acceptability, feasibility, and effect of psychosocial interventions,[28] through use of local and familiar music adapted to language and context, and for group music therapy this also involved tailoring to the individual residents' background. Nevertheless, the heterogeneity across countries underlines the importance of cultural and systemic factors and the challenges of multinational trials.

Both music interventions had positive effects on depressive symptoms at 3 months among those who received the interventions. These shorter-term effects might be related to dosage, as interventions were provided twice weekly during months 1–3, after which frequency was reduced to weekly sessions. Effects were also found among those with moderate or severe dementia, indicating that residents are more responsive to receiving support as the disease progresses.

The MIDDEL trial was considerably impacted by the COVID-19 pandemic, which had a substantial and disproportionate negative effect on symptoms and mortality of people living with dementia and on their caregivers.[28] Care homes were disrupted by lockdowns in an unprecedented way during the study, which restricted access to sites. Routine care was interrupted by intermittent closures and other preventive measures including mask wearing and limited group sizes, presenting unavoidable delays and complications to study procedures and adding to the workloads of care staff. Combined with an increase in social isolation and worsening of cognitive and non-cognitive symptoms among people living with dementia during the pandemic,[28] this is likely to have affected our outcome data, delivery of interventions, and their effects overall. Varying effects of the pandemic and related prevention measures across countries might have further contributed to increased international differences. Despite this, the target number of participants in MIDDEL was achieved, and no care home units were excluded after randomisation.

Previous trials of music interventions in dementia care involved smaller, more homogenous samples (14–121 participants[2,3,29–31]) and settings than in the current trial. The sample characteristics in MIDDEL suggest strong external

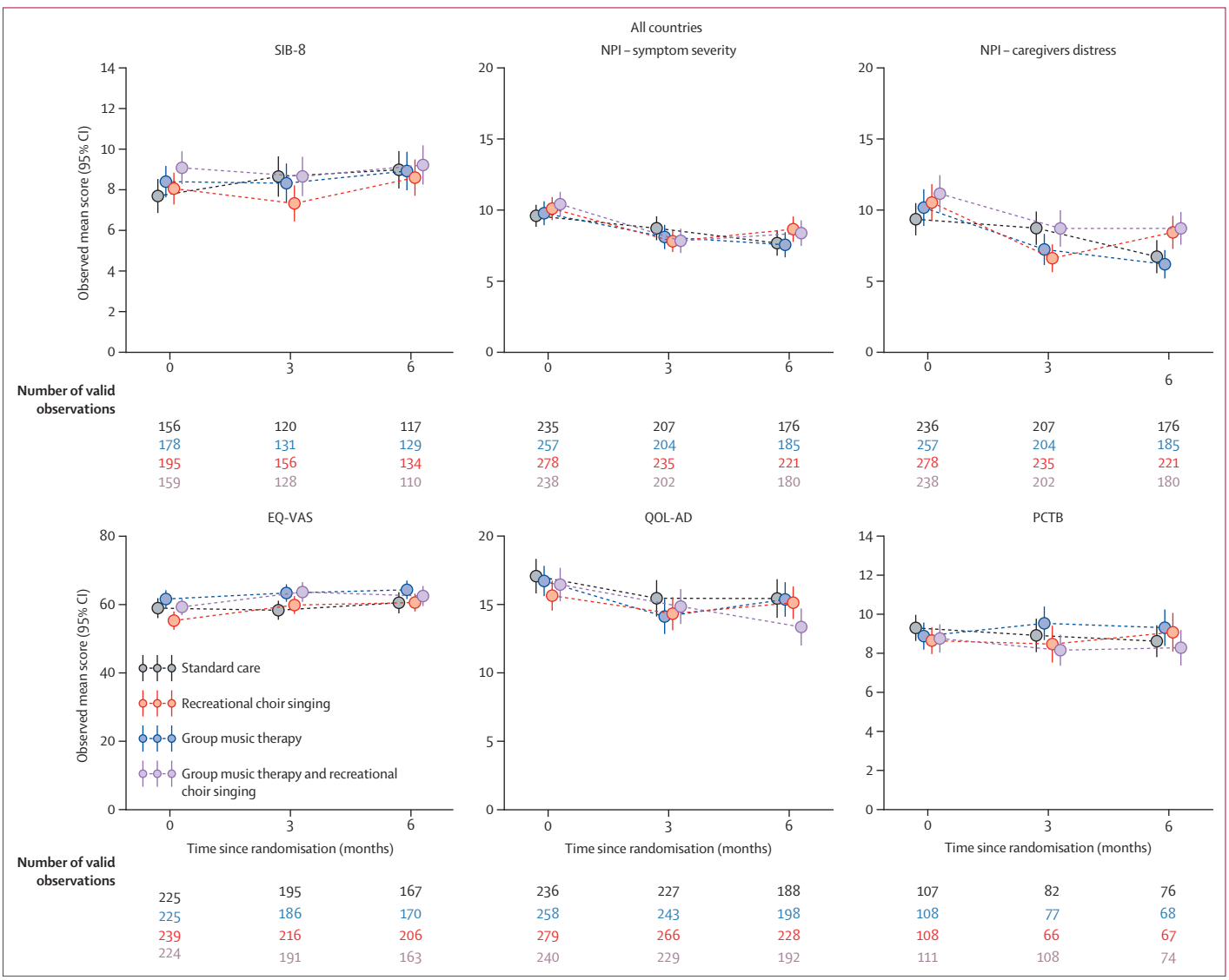

***Figure 3*: Secondary outcome data over 6 months**

Data are observed means and 95% CIs. SIB=Severe Impairment Battery. NPI=Neuropsychiatric Inventory. EQ-VAS=EuroQol Visual Analogue Scale. QoL-AD=Quality of Life in Alzheimer's Disease. PCTB=Professional Care Team Burden Scale.

validity for generalising the results to long-term residents with dementia and depressive symptoms across countries.[27] However, the variation in results by country shows that any effects of music interventions are not generalisable across contexts and underlines the importance of local implementation and contextual and cultural factors. The diverse sample in MIDDEL provides a broad perspective but suggests that future studies could benefit from focusing on narrower target groups, to avoid issues related to high variability cancelling potential effects. The mixed use of self-report and proxy allowed participation of those unable to respond to comprehensive instruments, but probably introduced discrepancies.[32] Furthermore, while assessors were masked, they would in some cases rely on input from informants who knew the participants well but were aware of the allocation. The use of observational assessment instruments relying on responses from care staff might also explain limited effects. It should be noted that further outcomes measured in MIDDEL, including those measured after more than 6 months, binary and time-to-event data, and biomarkers,[33] will be analysed and reported separately.

The findings of the current trial provide an important contribution to the existing evidence base by showing that these music interventions did not contribute additional effects to standard care at 6 months across a large sample of more than 1000 care home residents. Although we did not find statistically significant effects of group music therapy and recreational choir singing at our primary timepoint, these main findings do not necessarily negate the potential

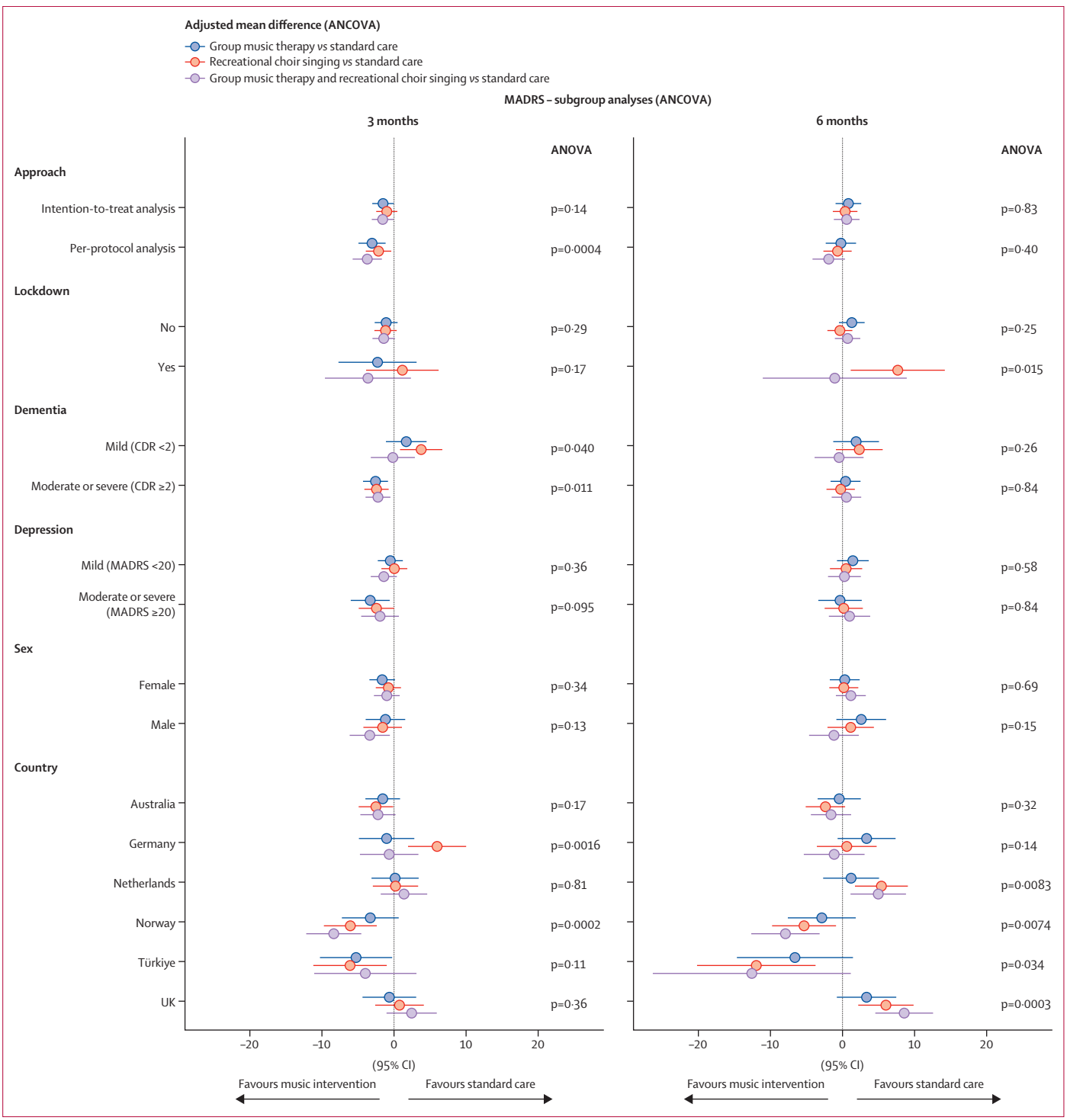

Figure 4: **Sensitivity and subgroup analyses**

Data are B (95% CI) coefficients in the ANCOVA for each subgroup. p values calculated from ANOVA (comparison of model with intervention versus model without intervention). CDR=Clinical Dementia Rating. MADRS=Montgomery-Åsberg Depression Rating Scale.

benefits of active music interventions, based on findings of beneficial shorter-term and sub-group effects. Although music interventions can be effective,[2] we do not yet understand well enough the underlying mechanisms of their effectiveness. Country, as a strong predictor, is likely a combination of many variables, including differences in

health-care systems and standard care, as the background against which we are measuring the add-on effects of music interventions. Other central factors include how the interventions themselves are structured and conducted (ie, obstacles to implementation[34] or intervention delivery and treatment fidelity[35]), and pathophysiological mechanisms (eg, stress[33] or music memory[36]). The inconsistent effects of recreational choir singing and group music therapy across countries therefore highlight a need for harmonisation of these interventions, as well as a need to better understand the link between their mechanisms, direct goals, and downstream effects.[5] Further moderators (individual-level [eg, music reward or music engagement];[36] cluster-level [eg, cost of living in a care home unit as an indicator for socioeconomic status[5]]) should also be considered.

In summary, while individual studies on music interventions in dementia care have provided compelling results, the current study is one of few large-scale clinical trials on the subject. It corresponds with other large-scale trials yielding inconclusive results, possibly attributable to heterogeneity in the sample receiving interventions that require tailoring to the individual participant and context.[25] The results of the current study, combined with previous evidence, suggest there is a need to further investigate the mechanisms through which music interventions work, with a focus on the specific contexts in which they are implemented.

Contributors

CG initiated the study and was the principal investigator of the international project until May 31, 2021. VS was the principal investigator for the international project (and was responsible for the sites in Norway) from this date until the completion of the project on Dec 31, 2023. BU (Türkiye), FAB (Australia), GK (Germany), and JS (UK) were national principal investigators. VS wrote the first draft of the manuscript with input from CG, JAs, and MG. FAB, HO-M, GK, JAb, JB, JDW, JN, JS, JT, NR, SJ, TW, UF, and Y-ECL developed intervention manuals or trained and supervised interventionists. AT, ACV, FAB, HO-M, JAb, JB, JDW, JN, NR, PAS-S, SJ, JS, UF, VS, and Y-ECL were involved in the implementation at care homes. CG, JA, JDW, MG, and VS were responsible for data management activities internationally. CG and JA conducted the statistical analysis and verified all underlying data reported in the manuscript. All authors had access to and contributed to interpreting the data, drafting the manuscript, approving the final version, and had final responsibility for the decision to submit for publication.

Declaration of interests

FAB is an associate editor for the *Journal of Music Therapy*, and JT is the former president of the Australian Music Therapy Association. All other authors declare no competing interests.

Data sharing

De-identified datasets (participant codes and outcome scores) generated during or analysed during the MIDDEL trial are stored in the publicly available repository OSF.

For the **de-identified data sets** see https://doi.org/10.17605/OSF.IO/TPDHU

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