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Singing for people with Parkinson's disease (Protocol)

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[Intervention Protocol]

Singing for people with Parkinson's disease

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To compare the efficacy and effectiveness of singing interventions with non-singing intervention or usual care on QoL, wellbeing, and speech and communication among people with PD. We will assess the QoL and the physical, psychological, and social health and wellbeing of people with PD who receive a singing intervention, compared to non-singing intervention or usual care.

BACKGROUND

For a glossary of terms see Table 1.

Description of the condition

Parkinson's disease (PD) is a complex chronic neurological condition that impacts upon a range of body functions. PD is characterised primarily by progressively worsening symptoms of movement abnormalities (e.g. bradykinesia, rigidity, and resting tremor). People with PD can also experience sleep disturbance, constipation, hyposmia, depression, and anxiety (Sutherland 2009). Furthermore, Parkinson's disease affects speech function due to the disturbances in muscular control of the speech mechanism (Herd 2012). The onset of PD is often unrecognised and it may take some years for people living with PD to be diagnosed (Mellick 2013).

Due to the chronic progressive nature of the disease, treatments for people with Parkinson's disease are complex and include medications, surgical procedures, and rehabilitation therapies such as physical, occupational, and speech therapy (Clarke 2007). Rehabilitation therapies focus on restoration of mobility and balance (physiotherapy), improvement of personal self-care activities (occupational therapy), and alleviation of communication difficulties (speech therapy) (Clarke 2007). Current pharmacotherapy can reduce Parkinson's symptoms, but is associated with unwanted side-effects, such as dyskinesia, dystonia, motor fluctuations, oedema, somnolence, dizziness, and hallucinations (Stowe 2008). These complications, and the increasing level of disability, significantly influence quality of life (QoL) in people with PD (Rahman 2008). Currently, there is no known cure and no therapy that can stall PD progression.

Description of the intervention

Singing is an accessible and popular form of musical activity. It involves physical functions, such as engaging the vocal apparatus and respiratory system (Leanderson 1988), as well as mental functions through emotional expression (Welch 2005). From a neurological point of view, singing is a complex activity that integrates auditory and sensorimotor processes in the brain (Wan 2010). When singing, speech-related mechanisms, such as respiration, phonation, articulation, and resonance, are directly stimulated (Sundberg 1987).

How the intervention might work

Studies have found that participation in group singing or choirs is associated with various health benefits across a wide range of outcome groups, including enhanced physical functions and mental, social, and spiritual wellbeing (Clift 2010a; Clift 2010b; Irons 2012; Irons 2016). Singing may enhance health and wellbeing through promoting neurochemicals such as dopamine, cortisol, serotonin, and oxytocin, as the structures of songs (e.g. melody, rhythm, and harmony) can induce a range of emotional and physical responses. For example, we may feel relaxed, peaceful, excited, or happy when singing certain songs (Chanda 2013).

Singing has also been reported to be beneficial for people with neurological conditions, such as PD, stroke, multiple sclerosis, and dementia (Sihvonen 2017). It is posited that singing offers an effective adjunct rehabilitation therapy for people with PD.

Quality of life

Several studies have suggested that participating in singing can enhance a person's QoL (Clift 2010a; Clift 2010b; Clift 2010c; Johnson 2013). Singing studies specifically for people with PD have also reported positive associations with enhanced QoL (Stegemöller 2017; Reagon 2016).

Physical health

While singing, facial muscles, vocal apparatus (i.e. the lungs, vocal cords in the larynx, mouth, and nasal cavities) and the whole respiratory system (i.e. the lungs, diaphragm, and intercostal muscles) are actively engaged to produce sounds (Sundberg 1987). Regular singing practice can reduce communication difficulties in people with PD (Evans 2012). Songs offer a range of pitch (low and high), dynamics (soft and loud), and emotional expressions through lyrics and harmony. Singing songs can provide an enjoyable exercise for people with PD, to retain or improve their communication skills. An increasing number of studies report positive impacts of singing on the speech parameters (e.g. increased loudness and phonation time) in people with PD (Evans 2012; Haneishi 2001; Kempler 2002; Shih 2012). Evidence also suggests that music can provide effective "auditory cueing" for people with PD in relation to improving movements (Ashoori 2015; Schaefer 2014; Thaut 2001). Rhythm and movements are naturally connected. Songs contain rhythm, which serves as natural timing for movements. A recent study has shown that listening to familiar songs can help people with PD to organise their walking movement efficiently (Leow 2015). Furthermore, through regular singing, it is suggested that people with PD can experience enhanced lung function (Di Benedetto 2009).

Psychological health

Managing the chronic and progressive nature of PD requires profound and prolonged adjustments to a person's lifestyle, which may impact psychosocial wellbeing. Depression and anxiety are the most common and significant comorbid conditions (Broen 2016; Dissanayaka 2010; Dissanayaka 2011). Group singing programmes have been demonstrated to promote resilience and provide effective coping strategies in adults who have faced adverse events (von Lob 2010). With regular singing activities (e.g. over six months), people have reported reduced psychological distress and improved wellbeing (Clift 2017). Songs can channel our senses through musical elements, such as rhythms, melodies, and harmonies, and enhance our emotional experience (Welch 2005). Through increased neurochemical activity (such as dopamine and oxytocin levels), singers experience pleasure, motivation, and a sense of reward (Chanda 2013).

Social health

Participating in group singing, such as a choir, can reduce isolation and provide social support. Taking part in group singing is reported to increase neurochemicals (in particular oxytocin), which is associated with bonding and social affiliation (Chanda 2013; Keeler 2015; Kreutz 2014). Singing with others can promote positive feelings, such as friendship and empathy, which are positively associated with a sense of wellbeing (Ryff 2008).

Why it is important to do this review

Non-pharmacological treatments for people living with PD play an increasingly important role (IQWiG 2015). As discussed above, evidence suggests that singing can be a beneficial complementary therapy for people with PD (Vella-Burrows 2012). The number of singing groups for people with PD in the community has been fast-growing in high-income countries, such as the UK, Australia, the USA, and Germany.

A recent review of music-based interventions in neurological rehabilitation highlighted the benefits of music for people with neurological conditions, including PD (Sihvonen 2017). However, the review did not examine the specific effects of singing for people

with PD. Another recent review on singing for people with PD reported benefits of singing in people with PD, but this was a narrative review and included non-randomised studies (Barnish 2016).

It is therefore timely to conduct a robust systematic review of the efficacy of singing for people with PD, including an examination of the effect of 'dose' of singing on relevant outcomes.

OBJECTIVES

To compare the efficacy and effectiveness of singing interventions with non-singing intervention or usual care on QoL, wellbeing, and speech and communication among people with PD. We will assess the QoL and the physical, psychological, and social health and wellbeing of people with PD who receive a singing intervention, compared to non-singing intervention or usual care.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs) of singing interventions versus non-singing interventions (e.g. listening to music), or usual care. Placebo is not possible due to the nature of the intervention. We will include trials that use both randomised and quasi-randomised methods of allocation.

Types of participants

Individuals with medically diagnosed idiopathic PD, receiving concurrent treatments. We will not place any restriction upon age, sex, ethnicity, drug therapy, other treatments, disease severity, or length of diagnosis. We will accept study authors' statements that participants were medically diagnosed.

Types of interventions

Singing interventions

Any singing interventions (e.g. group singing, choir, individual singing training) facilitated by professionals with a relevant qualification (e.g. music therapists, professional singing teachers, speech therapists, musicians, nurses, occupational therapists, or physiotherapists), with a minimum intervention length of two weeks. We will also consider singing programmes delivered via virtual technology, such as mobile phone applications or via websites, for inclusion and will assess for their comparability to other types of included singing interventions.

Comparison

Non-singing intervention (e.g. listening to music), or usual care without singing.

Types of outcome measures

Primary outcomes

- QoL (e.g. Parkinson's Disease Quesionnaire 39, World Health Organization Quality of life Queistonnaire-brief version, or other generic QoL measures, such as Short Form-36). PD-specific QoL measures and generic instruments may not be comparable, however, due to likely limited numbers of trials, we will include both PD-specific and generic instruments.
- Wellbeing assessments (e.g. Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS), Quality of Well-Being Scale Self-Administered (QWB-SA).

Secondary outcomes

- Speech and communication outcome measures (e.g. acoustic characteristics, standardised quantitative intelligibility assessments, standardised functional communication assessments).
- Respiratory function (e.g. forced vital capacity (FVC), forced expiratory volume-one second (FEV_1), maximal inspiratory pressure (MIP), and maximal expiratory pressure (MEP)).
- Depression and anxiety (e.g. Hospital Anxiety and Depression scale (HAD), Patient Health Questionnare-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), Depression Anxiety Stress Scales (DASS)).
- Motor function (e.g. PD motor impairment rating scales, such as Unified Parkinson's Disease Rating Scales (UPDRS) motor score, Part III, fall history, walking quantity and quality).

Adverse effects

We will include any time period of follow-up as stated in the studies. We will include singing versus usual care, or singing compared with another non-singing intervention, such as listening to music.

Search methods for identification of studies

Electronic searches

We will search the Cochrane Movement Disorders Group Specialised Trials Register. In addition, we will identify relevant articles through electronic searches, as described below.
In order to identify relevant studies we will use the following search terms.

- Parkinsonian Disorders or PD or Parkinsonism.
- Singing.
- Voice or vocal exercise or training.
- Choir.
- Music therapy.

We will search the following databases.

- Cochrane Database of Systematic Reviews (CDSR) EBM Reviews Ovid (2005 to present) (Appendix 1).
- Cochrane Central Register of Controlled Trials (CENTRAL) EBM Reviews Ovid (1991 to present).
- Database of Abstracts of Reviews of Effects (DARE). EBM Reviews Ovid (1991 to 2015).
- MEDLINE Ovid (1946 to present) (Appendix 2).
- Embase Ovid (1974 to present) (Appendix 3).
- CINAHL EBSCOhost (1937 to present) (Appendix 4).
- British Nursing Index ProQuest (1985 to present) (Appendix 5).
- PsycInfo Ovid (1806 to present) (Appendix 6).
- ClinicalTrials.gov (www.clinicaltrials.gov) (Appendix 7).
- World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) (www.who.int/trialsearch) (Appendix 8).
- ZETOC (The monitoring and search service for global research publications) (http://zetoc.jisc.ac.uk/) (Appendix 9).

We will not apply any date or language restriction. Translations of non-English resources will be carried out if necessary.

Searching other resources

We will attempt to identify other published, ongoing, and planned trials by performing the following.

- Inspecting references of all relevant studies.
- Searching trials registers such as ClinicalTrials.gov (clinicaltrials.gov) and the WHO ICTRP (apps.who.int/trialsearch).
- Handsearching relevant conference proceedings (e.g. speech pathologist conferences, PD/movement disorder conferences, music therapy conferences, etc).
- Contacting authors of relevant retrieved studies.

Data collection and analysis

Selection of studies

Two review authors (JYI and EC) will screen, by title and abstract, the articles identified by the search strategy. We will obtain the full-text articles of potentially eligible studies, and two review authors (JYI and EC) will screen these full-text articles. Any disagreements will be resolved by consulting a third review author (MKY). We will list any articles excluded after full-text assessment, and their reasons for exclusion, in a 'Characteristics of excluded studies' table. We will illustrate the study selection process in a PRISMA diagram.

Data extraction and management

Two review authors (JYI and MKY) will independently extract data onto a data collection form, including citation details, trial setting, inclusion and exclusion criteria, study population, intervention details, outcome measures, and results. All review authors involved in data extraction will be provided with detailed instructions. We will resolve any differences in opinion through discussion or, if necessary, through independent arbitration by a third review author (EC). We will attempt to contact study authors for any additional information needed. We will collect as many details as possible on participants including age at time of study, gender, disease duration, presence of speech problem(s), and PD medication.

Assessment of risk of bias in included studies

Two review authors (JYI and EC) will independently assess the methodological quality of the included trials using the criteria described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will assess the following items for each outcome in each included trial: sequence generation (randomisation), allocation concealment, blinding of outcome assessors, incomplete outcome data, and selective outcome reporting. Due to the nature of the interventions, blinding of participants and personnel is not applicable, however, as this causes a risk of bias, we will assess this criterion. Where required, we will attempt to contact corresponding authors to retrieve additional information. All information will be collected on the data collection form and any disagreements will be resolved through discussion.

Measures of treatment effect

We will calculate risk ratios (RR) with 95% confidence intervals (CIs) for dichotomous outcomes. We will calculate mean differences (MD) or standardised mean differences (SMD) for continuous outcomes, as appropriate. We will use Review Manager 5 software for all analyses (RevMan 2014).

Unit of analysis issues

The primary data for analysis in the included studies will be individual trial participants.

We will examine data from parallel-group RCTs and will aim to use data from intention-to-treat analyses.

If data are presented at different periods of follow-up, we will report the same outcome separately each time it is presented, based on the different periods of follow-up being reported. If the number of studies cannot adequately populate these analyses, we will select the longest period of follow-up for each study.

If the search identifies cross-over designs, we will utilise data from the first period of the trial only, given the degenerative nature of PD means a cross-over design is unlikely to be a suitable method for our review question. If the search identifies cluster-randomised trials, we will consult a statistician to assist in determining if the methods of analysis used in the trial were appropriate. In this instance, we will use the effect estimate and standard errors reported in meta-analysis. If the methods of analysis used in the trial were inappropriate, we will attempt to calculate the 'effective sample size' of the trial for inclusion in meta-analysis as outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*, section 16.3.4 (Higgins 2011). If this is not possible, we will report the results narratively.

Dealing with missing data

We will contact study authors to attempt to retrieve any missing data. We will consider studies to be at low risk of bias if study authors performed an intention-to-treat (ITT) analysis, or at high risk of bias if study authors did not perform an ITT analysis. If this is not possible due, for example, to the studies reporting aggregated data, we will impute missing data based on best-case and worst-case scenarios where possible. Where dropout is clearly identified for an outcome, we will report the true number of participants contributing to the data and will assess the potential impact of the missing data. Furthermore, we will assess blinding of outcome assessors and incomplete outcome data jointly.

Assessment of heterogeneity

We will consider heterogeneity firstly by considering the populations, settings, methods, and outcomes of the different studies. If clinically important heterogeneity is present, we will not pool the studies in a meta-analysis, but will describe them separately. We will examine the Chi^2 test and I^2 statistic values for each outcome. We will consider an I^2 statistic estimate of 50% or more, alongside a Chi^2 test P value of 0.1 or less, to indicate important heterogeneity. If there is heterogeneity, we will undertake pre-defined subgroup and sensitivity analyses and will re-examine the heterogeneity of these results separately.

Assessment of reporting biases

In the event of multiple publications of the same study, we will list the subsequent papers with the main paper and only enter data once. If there is uncertainty in this respect, we will attempt to contact the study authors. We will assess publication bias by examining funnel plots, if we have a sufficient number of included studies (at least 10). In the event of funnel plot asymmetry, we will assess possible reasons for this and report these descriptively.

Data synthesis

We will perform a random-effects model meta-analysis, as we anticipate that there is unlikely to be one true effect across the included studies due to variations of the intervention and other differences between studies. If we are unable to perform a meta-analysis due to substantial differences between the studies, or when only one study is identified for inclusion, we will report findings narratively, paying attention to the size, consistency, and direction of effect. Where we have included studies, we will create a 'Summary of findings' table for the comparison 'Singing compared to usual care without singing', and a 'Summary of findings' table for the comparison 'Singing compared to non-singing intervention'. We will include the primary outcomes and adverse effects in the 'Summary of findings' tables. We will use the GRADE considerations (study limitations, consistency of effect, precision, directness of evidence, publication bias, magnitude of effect, dose-response gradient, and plausible confounding that could reduce effect size) to assess the quality of the body of evidence generated by the included studies that contribute data to these outcomes. We will perform GRADE assessments using GRADEpro GDT software (GRADEpro 2015). We will specify all decisions to downgrade or upgrade the quality of the body of evidence in footnotes.

We will perform subgroup analyses as possible (as described below) if we identify heterogeneity.

Subgroup analysis and investigation of heterogeneity

- Duration of PD diagnosis (i.e. time since formal diagnosis < 10 years; 10 to 15 years; > 15 years).
- Severity of PD (according to Hoehn and Yahr staging of PD (Bhidayasiri 2012) , UPDRS).
- Age group (e.g. ≤ 65 years versus > 65 years) utilising mean ages in each trial (if we are unable to get full age spread from the study authors).
- Singing intervention length (e.g. brief (less than six weeks), short-term (6 weeks to 3 months), versus long-term (≥ six months)).
- Type of singing practitioner and their training (formally trained music or singing professional versus health or lay professional).

If a sufficient number of trials meet the inclusion criteria of this review to make this meaningful, we will perform these subgroup analyses whether we find heterogeneity is present or not.

Sensitivity analysis

We will perform sensitivity analyses, regardless of whether we identify heterogeneity or not, to assess the impact of missing data on the pooled estimate(s) of meta-analyses. If we find that heterogeneity is present, we will perform sensitivity analyses to assess the impact of the heterogeneity on the pooled estimate(s) of meta-analyses. Furthermore, if cross-over or cluster randomised studies meet the inclusion criteria of the review, we will conduct sensitivity analyses to assess the impact of inclusion of these designs on the pooled estimate(s) of meta-analyses, irrespective of whether heterogeneity is present or not.

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* *Indicates the major publication for the study*

ADDITIONAL TABLES

Table 1. Glossary

Terms	Definitions
Dysarthria	A collective name for a group of speech disorders resulting from disturbances in muscular control of the speech mechanism due to damage of the nervous system. It includes harsh and breathy voice quality, reduced overall loudness, mono-loudness, mono-pitch, reduced prosody, lower overall speaking pitch, slurred speech, illogical pauses, and short rushes of speech
Bradykinesia	Slowness of movement
Hyposmia	A reduced ability to smell and to detect odours
Dyskinesia	A movement disorder, characterised by involuntary muscle movements
Dystonia	A movement disorder in which a person's muscles contract uncontrollably
Motor fluctuations	Periods of the day with poor or no response to medication (off time). This alternates with periods of improved function (on time)
Oedema	A condition characterised by an excess of watery fluid collecting in the cavities or tissues of the body
Somnolence	Alternatively "sleepiness" or "drowsiness"; a state of strong desire for sleep, or sleeping for unusually long periods
Hallucinations	Someone sees, hears, smells, tastes, or feels things that don't exist outside their mind
Phonation	The production or utterance of speech sounds.

Table 1. Glossary (*Continued*)

Auditory cueing	The process whereby movement is synchronized to sound (Schaefer 2014).
Rhythm	The time-based pattern of music or sound, including beats and accents (Kennedy 2007).

APPENDICES

Appendix 1. CDSR/CENTRAL/DARE (EBM Reviews, Ovid) search strategy

#1 exp Parkinson's Disease/
#2 parkinson*.mp
#3 #1 OR #2
#4 exp singing/
#5 (singing OR singer).mp
#6 ((voice* or vocal*) adj3 (exercis* or train*)).mp
#7 (choir OR choral).mp
#8 exp music therapy/
#9 music therapy.mp
#10 #4 OR #5 OR #6 OR #7 OR #8 OR #9
#11 #3 AND #10

Appendix 2. MEDLINE (Ovid) search strategy

#1 exp Parkinsonian Disorders/
#2 parkinson*.mp
#3 #1 OR #2
#4 singing/
#5 (singing OR singer).mp
#6 ((voice* or vocal*) adj3 (exercis* or train*)).mp
#7 (choir OR choral).mp
#8 music therapy/
#9 music*.mp
#10 #4 OR #5 OR #6 OR #7 OR #8 OR #9
#11 #3 AND #10

Appendix 3. Embase (Ovid) search strategy

#1 exp Parkinsonian Disorders/
#2 parkinson*.mp
#3 #1 OR #2
#4 singing/
#5 (singing OR singer).mp
#6 ((voice* or vocal*) adj3 (exercis* or train*)).mp
#7 (choir OR choral).mp
#8 music therapy/
#9 music*.mp
#10 #4 OR #5 OR #6 OR #7 OR #8 OR #9
#11 #3 AND #10

Appendix 4. CINAHL (EBSCOhost) search strategy

#1 MH "Parkinsonian Disorders+"
#2 parkinson*
#3 #1 OR #2
#4 MH "singing"
#5 singing OR singer
#6 (voice* or vocal*) N3 (exercis* or train*)
#7 choir OR choral
#8 MH music therapy
#9 music therapy
#10 #4 OR #5 OR #6 OR #7 OR #8 OR #9
#11 #3 AND #10

Appendix 5. British Nursing Index (ProQuest) search strategy

parkinson* AND ((sing* OR singer) OR ((voice* OR vocal*) NEAR/3 (exercis* OR train*)) OR (choir OR choral) OR music therapy)

Appendix 6. PsycInfo (Ovid) search strategy

#1 exp Parkinson's Disease/
#2 parkinson*.mp
#3 #1 OR #2
#4 exp singing/
#5 (singing OR singer).mp
#6 ((voice* or vocal*) adj3 (exercis* or train*)).mp
#7 (choir OR choral).mp
#8 exp music therapy/
#9 music therapy.mp
#10 #4 OR #5 OR #6 OR #7 OR #8 OR #9
#11 #3 AND #10

Appendix 7. ClinicalTrials.gov search strategy

Condition/Disease: Parkinson OR parkinsonism OR parkinsonian
Other: sing OR signing OR singer OR voice exercise OR voice trainer OR vocal exercise OR vocal trainer OR choir OR choral OR music therapy

Appendix 8. World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) search strategy

Condition/Disease: Parkinson OR parkinsonism OR parkinsonian
Intervention: sing OR signing OR singer OR voice exercise OR voice trainer OR vocal exercise OR vocal trainer OR choir OR choral OR music therapy

Appendix 9. ZETOC search strategy

Parkinson* singing
Parkinson* singer
Parkinson* voice*
Parkinson* choir
Parkinson* choral
Parkinson* music therapy

CONTRIBUTIONS OF AUTHORS

J Yoon Irons drafted the protocol.

Esther Coren helped develop the protocol.

Manfred Gschwandtner designed the search strategy.

Megan K Young, Donald E Stewart, and George D Mellick provided comments on the protocol draft.

All protocol authors read and approved the final protocol version.

DECLARATIONS OF INTEREST

JYI and DES were part of an international, uncontrolled, feasibility study of a group singing programme (Sing to Beat Parkinson's®) with people with Parkinson's. Its findings will be presented at the 5th World Parkinson's Congress in Japan in June. All other authors (EC, MKY, MG and GM) have no known conflicts of interest.

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