Swallowing outcomes in dysphagia interventions in Parkinson’s disease: a scoping review

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Abstract

Objectives To identify all outcomes, their definitions, outcome measurement instruments (OMIs), timepoints and frequency of measurement applied in clinical trials in oropharyngeal dysphagia (OD) interventions in Parkinson’s disease (PD). This scoping review is the first stage of a larger project establishing a core outcome set for dysphagia interventions in Parkinson’s disease (COS-DIP).

Design Scoping review.

Methods Six electronic databases and one trial registry were searched without language restrictions until March 2022. Bibliography lists of included studies were also reviewed. Study screening and data extraction were conducted independently by two reviewers using Covidence. The scoping review protocol is registered and published (http://hdl.handle.net/2262/97652).

Results 19 studies with 134 outcomes were included. Trial outcomes were mapped to a recommended taxonomy for COSs and merged. 39 outcomes were identified. The most frequently measured were general swallowing-related outcomes, global quality-of-life outcomes and swallowing-related perceived health status outcomes. The applied outcomes, their definitions, OMIs, timepoints and frequency of measurement showed a high variability across all studies.

Conclusions The high variability of outcomes emphasises the need for an agreed standardised COS. This will inform clinical trial design in OD in PD, increase the quality of OD trials in PD and facilitate synthesising and comparing study results to reach conclusion on the safety and effectiveness of OD interventions in PD. It will not prevent or restrict researchers from examining other outcomes.

Trial registration number The COS-DIP study, including the scoping review, was registered prospectively with the Core Outcome Measures in Effectiveness Trials Database on 24 September 2021 (www.comet-initiative.org, registration number: 1942).

Introduction

Swallowing disorders (oropharyngeal dysphagia (OD)) are a common and clinically significant symptom in people with Parkinson’s disease (PD). The prevalence varies between 11% and 81% according to severity of the disease, definitions of OD and assessment tools used. Nearly 50% of people with PD experience aspiration, increasing the risk of developing pneumonia, which is a leading cause of death in people with PD.

OD interventions aim for safe, efficient and sufficient intake of food and fluids for patients while maximising quality of life (QoL) for the patient, their carers and their family. Clinical decisions on the safety and effectiveness of interventions are based on selected outcomes, thus the choice of outcomes to be measured and reported in clinical trials is critical. Furthermore, synthesising and comparing study results to direct treatment for people with OD in PD is necessary. Two recently published systematic reviews by Gandhi and Steele and López-Liria et al concluded that there is an ongoing significant...
lack of fundamental scientific evidence on the treatment of OD in PD. In an attempt to address this issue, Schindler et al established a consensus on the treatment of OD in PD. One conclusion made by the authors is that in neurodegenerative conditions such as PD, longer-term treatment effects and adverse events must also be assessed.

These three published reports demonstrate not only a deficiency of evidence on OD interventions in PD but argue that longer-term treatment effects and adverse events should be assessed consistently. Despite being intricately linked, these studies focus on the efficacy and efficiency of OD interventions themselves rather than on the outcomes that are targeted by the interventions.

Core outcome set for dysphagia interventions in Parkinson’s disease (COS-DIP)

A solution to these challenges is the development and use of an agreed standardised COS-DIP devised by key stakeholders including patients, healthcare professionals and clinical trialists. This will result in higher quality meaningful trials, which will enhance synthesising and comparing individual study results to reach conclusions on the safety and effectiveness of the interventions. It will not prevent or restrict researchers from examining other outcomes. In order to establish the COS-DIP, the first step is a scoping review of the literature on the applied outcomes in clinical trials in OD in PD. A scoping review was chosen as the most appropriate method to systematically map the research done in this area, as well as to identify any existing gaps in knowledge.

The objective of this scoping review was to report on all applied outcomes, their definitions, outcome measurement instruments (OMIs) and timepoints and frequency of measurement in (quasi-) randomised controlled trials (RCTs), controlled clinical trials (CCTs) and pilot/feasibility studies with control groups in OD in PD. This extracted information is brought together in a ‘long list of outcomes’ and will be used to inform the development of the COS-DIP. The following research questions were sought to be answered:

1. What are the outcomes of interest in clinical trials in OD in PD?
2. How are the outcomes in these clinical trials defined?
3. How are the outcomes in these clinical trials measured?
4. At which timepoints and at which frequency are the outcomes in these clinical trials measured?

Patient and public involvement

We did not involve patients or members of the public in the design or conduct of this scoping review. For all following stages of the COS-DIP we have established a study steering committee that will lead and conduct the development of the COS-DIP and includes a public research partner with PD.

Methods

Study protocol and registration

This scoping review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis extension for Scoping Reviews (PRISMA-ScR) checklist (see online supplemental file 1). A review protocol was devised beforehand and published online (http://hdl.handle.net/2262/97652). The COS-DIP study, including the scoping review, was registered prospectively with the Core Outcome Measures in Effectiveness Trials (COMET) Database on 24 September 2021 and was last revised on 20 December 2021 (www.comet-initiative.org, registration number: 1942).

Searches

A comprehensive search strategy, including two search strings (1) dysphagia and (2) Parkinson’s Disease, was devised with the assistance of a subject librarian. The databases AMED, CINAHL, EMBASE, MEDLINE, Web of Science, ProQuest Dissertations & Theses and trial registry Clinicaltrials.gov were searched from inception to 3 December 2021 and updated on 10 March 2022 (see online supplemental file 2). The reference lists of all included studies were screened for additional studies and study authors were contacted for additional information, if required.

Study inclusion and exclusion criteria

Studies were included if (1) participants had a diagnosis of OD and PD, (2) clinical interventions were aimed at improving swallowing or feeding difficulties, (3) at least one swallowing (related) outcome was measured and (4) the study design included at least one intervention and one control group (RCT, quasi-RCT, CCT or feasibility/pilot study with control group). Only studies with control groups were included as ultimately the COS-DIP will inform clinical trial design with a focus on RCTs so that meta-analysis of clinical trials in OD and PD will be feasible in the future. In accordance with the patient, concept and context framework, the following was applied:

► Patient: OD in idiopathic PD ≥ 18 years.
► Concept: any clinical intervention in PD.
► Context: any clinical context (all countries and healthcare settings, eg, acute care, primary healthcare and community setting).

Studies were excluded if they did not fit into the conceptual framework of the study or if a heterogeneous participant population including people with PD was studied but data could not be extracted for the PD subgroup solely. Finally, studies were excluded if no full text was available, eg, a conference abstract only, and authors were unable to provide sufficient information. No date or language restrictions were applied.

Study selection

Following the search, all identified citations were collated and uploaded to an online platform (www.covidence.org), where duplicates were removed automatically. A pilot test of a random sample of 25 titles and abstracts was carried out by 2 independent reviewers (JHirschwald and JHofacker) and achieved an agreement of 96% (preset cut-off was set at 75%). Following, all abstracts and titles and thereafter full texts, were screened independently by JHirschwald and JHofacker against the inclusion criteria. Any disagreement that arose between the reviewers at each stage of the selection process was either resolved through discussion or with an additional reviewer (MWalshe).

Data extraction strategy

Data was extracted independently from papers included in the scoping review by JHirschwald and JHofacker using a data extraction tool developed previously and applied by Hofacker. The extracted data includes details about the first author’s name, year of publication, country of origin, study design, population, sample size and applied outcomes. The data extraction form was trialled independently on three included sources by JHirschwald and JHofacker. As a result of discussion together with MWalshe, further parameters were added to the data extraction form: number of participants and dropouts, intention-to-treat analysis, age,
gender, PD severity, OD severity, intervention, comparator, OMIs, timepoints of measurement and frequency of measurement (see online supplemental file 3). Any disagreements that arose were resolved through discussion between JHirschwald and JHofacker, or with MWalshe in addition.

Data analysis and presentation
As no taxonomy for categorisation of outcomes in OD interventions specifically exists, a widely used taxonomy by Dodd et al \(^5\) was applied. This taxonomy was designed for trial outcomes and is applicable to all fields within medical research.\(^7\) It includes 5 core areas (death, physiological/clinical, life impact, resource use and adverse events) and 38 outcome domains.\(^15\)

The outcomes used in the included studies were extracted as verbatim following COS methodology as described in the COMET Handbook.\(^7\) All extracted data were categorised in an Excel spreadsheet also previously developed and applied by Hofacker\(^14\) and further adapted for the purpose of this study. It comprises information regarding core area of the outcome and outcome domain in accordance with the taxonomy by Dodd et al.\(^15\) outcome description as reported verbatim by study authors, definition of outcome, OMIs and timepoints and frequency of measurement. Furthermore, the amount and percentages of used outcomes within the respective core area and outcome domain were calculated.

Results
Search results
The literature search identified 2587 studies. After removal of duplicates, further 2328 records were excluded during title/abstract screening. Of the remaining 54 reports, 9 could not be retrieved as full texts and 27 did not meet the inclusion criteria in the full-text review (see online supplemental file 8). Additionally, two records were identified through citation searching, of which one was included. In total, 19 studies were included in this scoping review. Of these, 18 were in English and one in Chinese. The Chinese study was translated with the help of a translator and Chinese speaking Speech and Language Therapist. The results of the search and the study inclusion process are outlined in the PRISMA-ScR flow diagram in figure 1.\(^13\)\(^17\)

The included studies comprised 10 RCTs, 2 quasi-RCTs, 4 CCTs and 3 feasibility/pilot studies with control groups. Overall, 2124 participants were included with studies being published between the years 2000 and 2021, although all years were included in the search. Assessed interventions in the included studies were surface electrical stimulation (n=4), postural swallowing techniques (n=3), Expiratory Muscle Strength Training (n=3), application of biofeedback (n=2), repetitive transcranial magnetic stimulation (rTMS) (n=2), standardised swallowing training (n=2), deep brain stimulation (n=1), vocal training (n=1) and aural stimulation with capsaicin (n=1) (see online supplemental file 3 for the detailed characteristics of the included studies).

Within the 19 studies, 180 outcomes were identified. Of these, 46 outcomes were excluded for different reasons: (1) the outcomes were only assessed for determining whether the participants met the inclusion criteria for study participation but not the effect of the intervention, (2) neither the specific OMI nor results were reported or (3) due to missing information it was unclear what the outcome referred to (see online supplemental file 4).

Outcome areas
The majority of the 134 included outcomes belong to the outcome areas physiological/clinical (n=112; 83.58%) or life impact/functioning (n=19; 14.18%). One outcome was categorised to each of the outcome areas death, resource use and adverse events (n=1; 0.75% respectively).

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**Figure 1** Preferred Reporting Items for Systematic Reviews and Meta-analysis extension for Scoping Reviews flow diagram.
Outcome domains
As the taxonomy by Dodd et al was developed for clinical trials in medical research in general but not specifically for OD interventions, the outcome domains were adapted for the purpose of this scoping review. Figure 2 depicts the outcome domains from the included studies and the number of outcomes mapped accordingly.

Outcome subdomains
The outcome domain #9a comprises almost three quarters of all outcomes and the outcome domain #9b includes with over 8% the second most outcomes. In order to categorise these general outcome domains more precisely, recategorising according to subdomains was necessary. Outcome domain #9a was divided into the following five subdomains: (1) saliva management, (2) swallowing-related physiology, (3) swallow efficiency, (4) swallow safety and (5) neurological status. The outcome oropharyngeal dysphagia severity remained as was. Outcome domain #9b was split into two subdomains: (1) neurological findings and (2) voice.

Research question 1: what are the outcomes of interest in clinical trials in OD in PD?
The 134 included outcomes were merged to 39 outcomes due to overlaps or being identical. Table 1 presents the 'long list of outcomes' including the outcomes, subdomains, domains and outcome areas accordingly.

The outcome of most interest was penetration/aspiration measuring the depth of the entry of food and fluid into the larynx and airway. This was measured in 10 of the 19 studies. Oropharyngeal dysphagia severity was the second most often measured outcome (n=9). The top eight outcomes of interest in the included studies are depicted in figure 3. All other outcomes were measured one or two times.

Of these top eight outcomes, six belong to the outcome domain #9a general swallowing-related outcomes, whereas the other two belong to the outcome domain #30 global quality of life and #31a swallowing-related perceived health status.

Research question 2: how are the outcomes in these clinical trials defined?
Most definitions of the outcomes in the included studies vary widely. Thereof, 17 outcomes were not defined at all in any study, and 13 outcomes were defined by some studies but not by others. The outcomes swallowing-related hyoid bone movement and timing of oropharyngeal swallowing components were the most diverse defined outcomes. Each study used different parameters within these outcomes with either very specific or no definition. Outcomes that were assessed by using a scale or questionnaire were oftentimes not defined at all. Instead, the numerical scores from the scale or questionnaire were provided without explanation of what they related to. The outcome penetration/aspiration was defined in accordance with the definition by Rosenbek et al in 9 of 10 studies: ‘Penetration is defined [...] as passage of material into the larynx that does not pass below the vocal folds. Aspiration is defined as passage of material below the level of the vocal folds.’ There was no matching definition for any other outcome by at least two studies with different authors. The definitions of outcomes reported by Baijens et al were unsurprisingly in agreement given that both studies were conducted by the same main author group (see online supplemental file 5 for all definitions of outcomes).

Research question 3: how are the outcomes in these clinical trials measured?
Overall, the applied OMIs show high variability. Most of the outcomes in the outcome domain #9a were measured using instrumental assessments and either validated scales or scales designed for the purpose of the according study during videofluoroscopic evaluation of swallowing (VFS) (also referred to Modified Barium Swallow Study) or Fibreoptic Endoscopic Evaluation of Swallowing (FEES) or measuring it in milliseconds during electromyography.

The outcomes penetration/aspiration and swallowing-related quality of life were measured the most consistently. Eight of the ten studies used the Penetration–Aspiration-Scale (PAS) by Rosenbek et al during VFS and/or FEES. One study did not report the scale that was used to measure the outcome during VFS and another study used a self-designed 4-point scale. The outcome swallowing-related quality of life was measured through the Swallowing Quality of Life (SWAL-QOL) Questionnaire in six studies, whereas one study additionally assessed this outcome through the MD Anderson Dysphagia Inventory. The outcome self-perception of swallowing was measured by the Swallowing Disturbance Questionnaire three times and the Dysphagia
Severity Scale (DSS) and Arabic Dysphagia Handicap Index once each.

The outcome oropharyngeal dysphagia severity was the outcome measured most differently across all included studies. In order to assess the outcome either validated scales or self-designed scales for VFS and/or FEES, the Standardized Swallow Assessment or a Clinical Swallow Evaluation were conducted. The OMs of death and hospitalisation were not described and while it may seem self-explanatory, their methods of recording were not clear (see online supplemental file 6 for the applied OMs).

**Research question 4: at which timepoints and at which frequency are the outcomes in these clinical trials measured?**

In the outcome domains #1, #22, #35 and #38 only one study assessed the outcomes death, aspiration pneumonia, hospitalisation and adverse events, respectively. These were measured

Figure 3 Number of studies measuring each outcome in clinical trials in oropharyngeal dysphagia in Parkinson’s disease.
continuously over a period of 3 months without further details provided by the authors. All remaining outcomes in the outcome area physiological/clinical were measured in the included studies one to five times either during or pre to post and/or with one to two follow-ups. The timepoints post intervention ranged from 5 min to 6 months.

The outcomes in the outcome area life impact/functioning were measured 1–36 times during, pre and/or post with follow-up assessments 2 weeks to 6 months post intervention. The outcome participant’s adherence to intervention was assessed weekly over a period of 3 months, hence 36 times in 1 study. The outcome self-perception of swallowing was measured differently at varying timepoints and frequency across the included studies. For example, 1 study assessed the outcome through the DSS after each session, hence 13–15 times, whereas the other 4 studies assessed it 2, 3 or 5 times. Only the outcome participant’s satisfaction with the intervention was measured once during or 2 weeks post intervention.

Overall, most outcomes were measured at least pre and post intervention with frequencies from one to four times. If the outcome was measured only once this was usually during the intervention, for example, rTMS (see online supplemental file 7 for all timepoints and frequency of measurements).

Discussion

In this scoping review, 19 clinical trials that investigated OD interventions in PD with 134 outcomes were included. Outcomes were merged to 39 final outcomes in 13 outcome domains. Outcomes of interest, definitions, OMIs, timepoints and frequency of measurement varied highly across the included studies. This scoping review identified relevant challenges within the included studies.

One major challenge in the included studies is the lack of information on outcomes, their definitions, and OMIs and omitted outcomes. For example, three studies did not report on outcomes in detail if there were no differences between the intervention and the control group. In two other studies, the authors did not report why outcomes were omitted. Incomplete reporting of research methods (eg, what was measured and how it was measured) and selective reporting of findings (eg, omitted outcomes) decrease the transparency of the research studies and raise questions about the applicability of the findings and study reporting practices. This heightens the risk that results lack credibility and studies are not easy to replicate and reproduce.

This is especially problematic in healthcare research involving OD interventions in PD where the outcomes of these clinical trials are essential for decision-making, such as the safety and effectiveness of the intervention.

Another identified challenge in the included studies is that some of the outcomes that were previously identified in the literature as relevant for people with OD and PD were not or rarely assessed. Only one study included the outcome voice as they assessed the effect of vocalisation training in improving drooling in people with PD. However, three pilot studies have previously shown that cross system effects through an intensive, evidence-based voice and speech treatment (Lee Silverman Voice Treatment, LSVT LOUD) in people with PD can improve swallowing. These studies suggest that training voice and speech may improve swallow function as well. Concurrently, dysphagia therapy might affect voice and speech in PD. Therefore, voice as an outcome in clinical trials in OD in PD might be relevant to assess.

Just 6 of the 19 included studies assessed swallowing-related quality of life and five studies included self-perception of swallowing as patient-reported outcomes. This is a relatively small number, as patient-reported outcomes are considered critical for evidence-based practice and for assessing treatment effectiveness. It should be noted that specifically in people with PD the self-assessment may differ from objective or investigator-reported outcomes due to sensorimotor deficits and hence, both types of assessments should be included.

Outcomes that were not typically measured but may be considered relevant included parameters associated with cough, hydration and nutrition. People with OD in PD are at high risk of developing malnutrition and dehydration. This can further impair swallowing function and delay the rehabilitation process. It can also increase the risk of medical complications or even mortality. Furthermore, impaired cough (dystussia) reduces airway protection as material entering the airway might not be expelled effectively. Dystussia often coexists with OD in people with PD and therefore the risk of aspiration and pneumonia is increased, but also QoL can be decreased. This is not surprising as both coughing and swallowing are sensorimotor behaviours that overlap in anatomy and neuroanatomical substrates. Therefore, outcomes associated with hydration, nutrition and cough might be relevant to assess in future OD interventions in PD.

A further interesting finding in this review is that only one study assessed outcomes pertaining to the outcome areas of death, resource use and adverse events. Assessing and reporting adverse events in RCTs is crucial for determining the safety of an intervention, but is less focused on than assessing and reporting efficacy and effectiveness in these trials. The outcome area adverse events might comprise numerous outcomes, which typically are not predefined as they are usually unknown before commencing a study. Furthermore, only assessing if adverse events are present or absent is regarded as insufficient. Additional information on the severity, timing, duration and number of occurrences of the events is required and thus, making the assessment, reporting and analysis of these outcomes more laborious and possibly inconsistent. Death might be incorporated as an outcome of adverse events. In OD interventions in PD, the assessment and reporting of death might be more relevant than currently considered. As stated before, dysphagia and dystussia increase the risk of aspiration and hence pneumonia, which is a leading cause of death in people with PD. Therefore, addressing this outcome area in future clinical trials in addition with adverse events might be relevant. The reporting of adverse events in clinical trials might further be improved by the adoption of the Consolidated Standards of Reporting Trials harm extension guideline.

Following the Dodd et al taxonomy, the outcome area resource use comprises the outcome domains economic, hospital, need for further intervention and societal/carer burden. Of these, only hospital in terms of length of hospital stay was assessed in one of the included studies. This outcome area might be under-represented in OD in PD studies. A recent systematic review showed that the presence of dysphagia increases the hospital length of stay, regardless of admission cause. Furthermore, this also increases the monetary costs by over 40% in patients with dysphagia compared with non-dysphagic patients. In addition, pneumonia is one of the most common reasons for emergency hospital admission in patients with PD, making patients with OD in PD more likely to be admitted to hospital and increase overall healthcare costs. Additionally, Perry et al found that providing care for a person with OD in PD reduces the carer’s QoL due to an increased burden. In future studies on OD in PD, it might be important to assess outcomes related to carer burden as ultimately, a less burdened carer might improve a PD person’s health outcomes and QoL.
Lastly, the use of unvalidated OMIs (in general or for the specific patient population) in the included studies comprised a further challenge. Validated OMIs are important to ensure that the tool is measuring what it is supposed to measure, and hence, that the results are valid.

Strengths and limitations of the study
In order to categorise the outcomes, the taxonomy devised by Dodd et al was applied as recommended by the COMET Handbook. This is widely implemented in outcome research and facilitates consistent use of clinical outcome terms. However, the taxonomy was devised largely for medical research, making it less specific to OD interventions. Furthermore, a possible limitation in this review is the restriction of the review to include clinical trials only, but this was based on the fact that the focus of the COS-DIP is a COS for clinical trial design.

Conclusion
This is the first scoping review that has systematically extracted and categorised all outcomes in clinical trials in OD interventions in PD. We identified high variability in included outcomes in addition to outcomes that were rarely measured or not measured at all. Furthermore, a lack of information on outcomes, such as definitions, OMIs and timepoints of measurement, was identified which can affect a study’s replicability, credibility and decrease its validity. Additionally, in some of the included studies, outcomes mentioned as part of the study’s research question were later omitted and hence pose a risk of reporting bias and skewing individual study results.

Through the development of the COS-DIP, the minimum core outcomes to be measured and reported in all future OD interventions in PD will be agreed on and advice on how and when to measure these will be provided. Ultimately, this will increase the quality of OD trials in PD and reduce research waste. It will not prevent or restrict researchers from examining other outcomes.

Deviation from protocol
In addition to (quasi-) RCTs and CCTs also, feasibility/pilot studies with control groups were included in this scoping review. This allows for inclusion of all clinical trial designs. No other deviations were made from the study protocol.

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Contributors
JHirschwald drafted the manuscript. J Hofacker was second reviewer. Discussions on inclusion/exclusion of studies were discussed and solved with MWalshe. The long list of outcomes was agreed on by all authors. All authors critically appraised and edited the manuscript. All authors read and approved the final manuscript. MWalshe is the guarantor for this study.

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Supplemental material
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References
Original research


