

# Identification of eating, drinking and swallowing difficulties for people living with earlystage dementia: a systematic review

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#### REVIEW



# Identification of eating, drinking and swallowing difficulties for people living with early-stage dementia: A systematic review

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#### Abstract

**Background:** The prevalence of dementia is increasing, bringing a range of challenges, such as eating, drinking and swallowing (EDS) difficulties, that are associated with aspiration, which can be fatal. Early identification of EDS difficulty in early-stage dementia could prevent complications, but reliable indicators are needed to help develop pathways to support the diagnosis. Previous reviews of this area require updating.

**Aims:** To identify reliable and clinically measurable indicators of EDS difficulty used in early-stage dementia.

**Methods & Procedures:** A systematic search was conducted using common databases (MEDLINE, EMBASE and PsychInfo). Articles reporting indicators of EDS difficulty in early-stage dementia or mild cognitive impairment were included. The reliability of included studies was critically appraised using the risk of bias tools. Study outcomes were narratively reviewed by considering the reliability, clinical measurability and applicability of EDS indicators to early-stage dementia.

**Outcomes & Results:** Initial searches returned 2443 articles. After removing duplicates, limiting to English language and human studies, 1589 articles remained. After reviewing titles, 60 abstracts were reviewed, yielding 18 full-text articles. A total of 12 articles were excluded that did not report at least one indicator of EDS difficulty in early-stage dementia, or where the reported association was not strong. Six included studies that reported eight indicators of EDS difficulty in early-stage dementia (four studies including people with Alzheimer's disease). On the balance of measurability, reliability and applicability, the most promising indicators of EDS difficulty were: delayed oral transit, rinsing ability, sarcopenia and polypharmacy. Additional, less reliable and applicable indicators included: always opened lips and non-amnestic mild cognitive impairment, especially in men. The delayed pharyngeal response is subjectively measured when

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instrumental assessment is not available and the 'candy sucking test' cannot be recommended because there is an inherent choking risk.

**Conclusions & Implications:** EDS difficulty in early-stage dementia can be highlighted by indicators that could be combined to create enhanced pathways to support the early identification of EDS difficulties for people living with early-stage dementia with a view to preventing complications and facilitating informed discussions regarding wishes in the event of further deterioration. Exploring the experiences of people living with dementia and their families' perspectives on potential indicators of EDS difficulty may add to the existing evidence base.

#### KEYWORDS

dementia, drinking, eating, swallowing, systematic review

#### WHAT THIS PAPER ADDS

What is already known on the subject

• Early identification of EDS difficulty in early-stage dementia may prevent complications, but more reliable and clinically measurable indicators of EDS difficulty are needed to help develop pathways to support diagnosis.

What this paper adds to existing knowledge

A comprehensive range of studies related to EDS identification in early-stage dementia have been selected and reviewed. Across six included studies, the most promising indicators of EDS difficulty in early-stage dementia included delayed oral transit, poor rinsing ability, presence of sarcopenia and polypharmacy.

What are the potential or actual clinical implications of this work?

• This study could help to develop pathways to support the early identification of EDS difficulties for people living with early-stage dementia with a view to preventing complications and facilitating informed discussions regarding wishes in the event of further deterioration.

#### INTRODUCTION

The Global Burden of Diseases, Injuries, and Risk Factors Study reported that the prevalence of dementia has more than doubled from 20.2 million in 1990 to 43.8 million in 2016 (Nichols et al., 2019).

Over half of the people living with dementia may have eating, drinking and swallowing (EDS) difficulties (Alagiakrishnan et al., 2013). Deterioration in cognitive and executive function in early-stage dementia may predispose to EDS difficulty (Rogus-Pulia et al., 2015), with around 20% of people living with early-stage dementia being affected (Kai et al., 2015).

EDS difficulty in dementia is a significant independent risk factor for poorer outcomes including aspiration pneumonia and malnutrition (Paranji et al., 2017). Although there are few proven interventions to treat established EDS difficulty in people living with dementia, early identification of EDS difficulty may allow for modification of risk (Abdelhamid et al., 2016). Speech and language therapists (SLTs) primarily use compensatory strategies in this client group and frequently cite the need for family and care staff training in mealtime support (Egan et al., 2020).

Expert opinion suggests that impairment in self-feeding (Rogus-Pulia et al., 2015) and altered sensations

(i.e., gustatory functions such as taste perception and flavour preferences) are early signs of EDS difficulty (Winchester & Winchester, 2016). However, opinions are sometimes challenged. Hence, more reliable and clinically measurable indicators of EDS difficulty are needed to help develop pathways to support the diagnosis. Previous reviews of this area have not focused on the identification of EDS difficulty in early-stage dementia and have considered studies including people with all stages of dementia. The literature searches also require updating for newer evidence (Affoo et al., 2013; Alagiakrishnan et al., 2013). This area of practice involves a range of factors, early indicators, signs and symptoms that can be presented together. Here, we use the term indicator to cover all potentially relevant factors that have been associated with the pathophysiology of EDS difficulty.

#### CLINICAL APPLICATION

The model for supporting people with dementia and their families requires support services to be seamless, accessible and proactive (Department of Health, Social Services & Public, Safety, 2011). If people living with dementia and EDS difficulty are identified, SLTs can implement compensatory strategies, and initiate family and care staff training (Egan et al., 2020). There is preliminary evidence to suggest that the caregiver approach to people living with dementia may influence aspiration risk (Gilmore-Bykovskyi and Rogus-Pulia, 2018) and for carers, early identification of EDS difficulty may help reduce stress (Papachristou et al., 2013) and isolation associated with this problem (Gillies, 2012). Early identification of EDS difficulty could act as a trigger for advance care planning to establish the wishes of people living with early-stage dementia, in the event of further deterioration. For example, some may refuse future treatments, such as artificial nutrition and hydration (Anantapong et al., 2021). To integrate existing information and enable rational decision-making, an updated review could establish whether findings are consistent and can be generalized across populations, settings and stages of disease (Mulrow, 1994).

#### AIM AND OBJECTIVES

The overall aim was to identify reliable and clinically measurable indicators of EDS difficulty in early-stage dementia. This was addressed via three objectives, each with respect to populations of early-stage dementia:

 To find studies reporting on early identification of EDS difficulty.

- To discover reliable indicators of EDS difficulty.
- To review the clinical measurability of specific indicators of EDS difficulty.

#### **METHODS**

A systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021). Difficulty in EDS was previously termed *dysphagia* (Robertson et al., 2018). For the purposes of the review, the term *EDS difficulty* is used to describe what is termed *dysphagia* in the included studies. Early-stage dementia is considered to be consistent with a clinical dementia rating of 1 or with the descriptor *mild dementia* (Morris, 1993).

# Search strategy

A search for relevant literature was conducted on the Ovid platform using the MEDLINE, EMBASE and PsychInfo databases using the search terms in Appendix A. Duplicate articles were removed, and the limitations set were English language and human studies. A review of article titles was performed to identify potentially relevant studies before assessing article abstracts and then performing full-text reviews to identify included studies.

## Inclusion and exclusion criteria

Articles reporting indicators of EDS difficulty in studies including people with early-stage dementia or mild cognitive impairment were included, regardless of date of publication. The rationale for including mild cognitive impairment is that it can precede dementia (Winchester & Winchester, 2016) and EDS difficulty is recognized at this stage of cognitive decline (Takahashi et al., 2019). Studies were excluded that did not report at least one indicator of EDS difficulty in early-stage dementia, or where the reported association between indicators and EDS difficulty was not considered strong (Akoglu, 2018). Conference proceedings and abstracts without full text were excluded due to a lack of information to assess the risk of bias.

#### Data extraction

Data were extracted using a standard template. Resulting tables were checked by the authors for accuracy and completeness. Findings were cross-checked with previous reviews (Affoo et al., 2013; Alagiakrishnan et al., 2013).

# Critical appraisal

The reliability of the studies was formally assessed depending on the study type using the following risk of bias tools: Newcastle–Ottawa scale (Wells et al., 2013), the National Heart, Lung, and Blood Institute Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (NHLBI, 2021), and the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) (Whiting et al., 2011). Included studies were classified in terms of evidence level by the Scottish Intercollegiate Guidelines Network grading system (SIGN, 2015). Studies were not excluded on the basis of risk of bias or quality.

# Narrative review

There was clinical heterogeneity in the included studies so meta-analysis was not possible, therefore the studies and findings on critical appraisal were narratively reviewed by considering the reliability and bedside (i.e., non-instrumental/non-invasive) clinical measurability of reported indicators of EDS difficulty. Narrative review also considered the applicability of studies reporting indicators to the early-stage dementia population. A narrative review aims to summarize the literature and provide a structured summary of a defined topic (Baethge et al., 2019). Robustness was enhanced through critical appraisal of included studies using a risk of bias tool, specific to each study type. Findings were agreed by consensus.

#### RESULTS

#### Search results

The search returned 2443 articles. After removing duplicates and limiting to English language and human studies, the titles of 1589 articles were reviewed for relevance leaving 60 abstracts that were reviewed. A total of 18 full-text articles were further reviewed (see the flow chart in Figure 1).

Two studies were excluded that only compared different forms of dementia with each other in terms of swallowing and EDS characteristics as opposed to identifying specific indicators of EDS difficulty (Ikeda et al., 2002; Suh et al., 2009). Three other studies were excluded as they included no participants with early-stage dementia (de Correia et al., 2010; Horner et al., 1994) or where no breakdown of dementia severity in participants was provided (Wada et al., 2001).

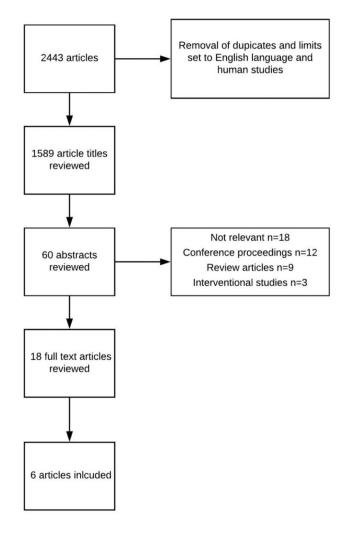


FIGURE 1 Study selection flow diagram following PRISMA guidelines

Three studies that did not report an indicator of EDS difficulty were excluded (Goes et al., 2014; Miarons et al., 2018; Suto et al., 2014). Two studies in which a reverse relationship was assessed were excluded (Edahiro et al., 2012; Takagi et al., 2017). For example, one of these two studies assessed for associations with decreased skeletal muscle in people living with dementia and identified EDS difficulty as having an independent association (Takagi et al., 2017). The other study assessed for associations with the ability to self-feed in people living with dementia and identified EDS difficulty as having an independent association (Edahiro et al., 2012).

In a further study, the Mann Assessment of Swallowing Ability had a statistically significant negative correlation with aspiration on videofluoroscopic swallowing studies, but the strength of the association (Spearman's Rho = -0.349) was not strong enough to consider the assessment an indicator (Ji et al., 2019). The strength of this association would be considered moderate (Akoglu, 2018).

One study was excluded that reported an indicator of EDS difficulty in early-stage dementia (reduced hyolaryngeal elevation), but assessment of swallow was performed in a supine position. Swallowing assessments were made in the supine rather than upright position because the study also involved the use of functional magnetic resonance imaging scans performed during swallowing. EDS is not typically assessed when lying flat, therefore this study was not considered further (Humbert et al., 2010).

A total of six studies were included, and the references of these studies were investigated for additional potentially relevant publications, but none was identified (Figure 1). Eight indicators of EDS difficulty were reported across the six included studies (Mori et al., 2017; Naruishi et al., 2018; Özsürekci et al., 2020; Priefer & Robbins, 1997; Sato et al., 2014; Yang et al., 2014) (Table 1).

# Narrative review of findings

The six studies generate several indicators associated with EDS difficulty.

# Delayed oral transit and delayed pharyngeal response

In a good-quality case control study by Priefer and Robbins (1997) (SIGN evidence level 2+), it was identified that compared with healthy control subjects, delayed oral transit and delayed pharyngeal response were features of swallowing impairment in mild Alzheimer's disease, considered equivalent to early-stage dementia (McGee et al., 2017). However, measurements of oral transit and pharyngeal response were taken on videofluoroscopic swallowing studies, which limits applicability to clinical measurement of these features at the bedside. Despite this, they are key findings that resonate with other indicators of EDS difficulty that may reflect impairment in oral transit, such as lack of rinsing ability (Sato et al., 2014). The relationship of these swallowing impairments (i.e., delayed oral transit and delayed pharyngeal response) with more advanced deterioration in swallow (i.e., penetration or aspiration) was not demonstrated. This suggests that delayed oral transit and delayed pharyngeal response predate significant swallowing impairment and are as such potentially useful to identify.

# Lack of rinsing ability

In a good quality cross-sectional study from Sato et al. (2014) (SIGN evidence level 2+), the easy-to-measure lack of rinsing ability was demonstrated to have an

independent relationship on logistic regression analysis with EDS difficulty. People who could rinse rhythmically sequentially without leaking water were defined as having 'better' function, whereas those who could not were defined as 'worse'. Therefore, rinsing ability would be easy to classify at the bedside. However, EDS difficulty was defined only by water swallow test, which is less sensitive and specific than either of the gold standard reference tools of videofluoroscopic swallowing study or fibreoptic endoscopic evaluation of swallow. The authors also included patients with all degrees of severity of Alzheimer's disease and the combined prevalence of poor rinsing ability in 18% was reported in the mild and moderate Alzheimer's disease populations. It was therefore unclear how common rinsing ability would be in early-stage dementia. Despite this, the multivariate analysis performed by Sato et al. (2014) controlled for clinical dementia rating scale (i.e., dementia severity), which suggests that rinsing ability is likely an indicator of EDS difficulty across all severities of Alzheimer's disease, including those with early-stage disease.

# Sarcopenia and polypharmacy

In another good quality cross-sectional study by Özsürekci et al. (2020) (SIGN evidence level 2+), the easily measurable factors of sarcopenia and polypharmacy demonstrated significant and independent relationships with EDS difficulty on videofluoroscopic swallowing studies. This study covered the full range of Alzheimer's disease severity but excluded patients more likely to have severe dementia, for example, those unable to comply with instructions. The applicability of this study to the target population of early-stage dementia therefore appears relatively good. The prevalence of polypharmacy and sarcopenia (probable sarcopenia, sarcopenia and severe sarcopenia) in the mild Alzheimer's disease group was high at 65% and 61%, respectively. The European Working Group on Sarcopenia (Cruz-Jentoft et al., 2019) defines three levels: (1) probable sarcopenia with low muscle strength; (2) sarcopenia: low muscle strength in combination with reduced muscle quality; and (3) severe sarcopenia: low muscle strength, reduced muscle quality and decreased physical performance. Strength is assessed using a manual handgrip dynamometer. Quality is estimated using bioimpedance to derive muscle mass. Performance is assessed by time to walk 4 m at usual speed (more than 5 s regarded as reduced performance) (Özsürekci et al., 2020).

In addition, the logistic regression analysis for independent predictors of EDS difficulty controlled for clinical dementia rating scale. The factors identified are likely applicable to the mild Alzheimer's disease group in the study.



Summary of evidence and critical appraisal showing useful support for certain factors that may indicate or predict EDS difficulties TABLE 1

•			•	•			
Study and country	Identifier of EDS difficulty (effect size in multivariate analysis)	Study population	Prevalence of identifier	Evidence level	Study assessment tool	Study assessment score	Clinical measurability
Mori et al. (2017) Japan	Candy sucking test	Alzheimer's disease ( $n = 23$ ) Median MMSE 10	n.a.	2-	QUADAS-2	ı	Poor
Naruishi et al. (2018) Japan	Opened lips at all times (OR = 1.99, 95% CI = 1.1–3.7)	Cognitive impairment ( $n$ = 698) No cognitive impairment ( $n$ = 476)	n.a.	2-	NHLBI	7/11	Good
Özsürekci et al. (2020) Turkey	Sarcopenia (OR = 4.9, 95% CI = 1.2–19.6)	Alzheimer's disease: Mild $(n = 26)$ Moderate $(n = 31)$ Severe $(n = 19)$	Probable sarcopenia 31% Sarcopenia 15% Severe sarcopenia 15%	2+	NHLBI	8/11	Good
Özsürekci et al. (2020) Turkey	Polypharmacy (OR = 6.1, $95\%$ CI = $1.6-23.9$ )	Alzheimer's disease: Mild $(n = 26)$ Moderate $(n = 31)$ Severe $(n = 19)$	%59	5+	NHLBI	8/11	Good
Priefer and Robbins (1997) USA	Delayed oral transit	Mild Alzheimer's disease $(n = 10)$ Controls $(n = 15)$	Not reported	2+	Newcastle- Ottawa	6/8	Good
Priefer and Robbins (1997) USA	Delayed pharyngeal response	Mild Alzheimer's disease $(n = 10)$ Controls $(n = 15)$	Not reported	2+	Newcastle- Ottawa	6/8	Poor
Sato et al. (2014) Japan	Rinsing ability (OR = 4.8, 95% CI = 1.9–12.1)	Alzheimer's disease: Mild $(n = 26)$ Moderate $(n = 68)$ Severe $(n = 61)$	18% (mild and moderate)	2-	NHLBI	6/11	Good
Yang et al. (2014) Korea	Non-amnestic mild cognitive impairment in men (OR = 3.77, 95% CI = 1.1–12.7)	Cognitive impairment ( $n = 81$ ) No cognitive impairment ( $n = 334$ )	n.a.	5-	NHLBI	7/11	Poop
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Note: MMSE, Mini-Mental State Examination; NHLBI, National Heart, Lung, and Blood Institute Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies; OR, odds ratio.

# Non-amnestic cognitive impairment

Mild cognitive impairment in the absence of memory impairment (i.e., non-amnestic cognitive impairment) was reported to have a significant and independent relationship with EDS difficulty in patients with mild cognitive impairment but only in men. Memory impairment would be relatively easy to assess and measure. However, an important criticism of Yang et al. (2014) is the use of an unvalidated swallowing assessment for defining EDS difficulty. Although the study otherwise scored fairly using the risk of bias tool for cross-sectional studies (NHLBI, 2021) the risk of bias was considered high (SIGN evidence level 2-). The number of individuals with mild cognitive impairment in the study was also low (cognitive impairment n =81 versus no cognitive impairment n = 334), thus reducing its applicability to the target population of interest. While a potentially interesting observation was identified in the study, one must be mindful that this study describes an association between the type of cognitive impairment and EDS difficulty (Yang et al., 2014). It seems biologically implausible that the type of cognitive impairment would be a causative factor in EDS difficulty, particularly as it is only a feature in male patients.

# Open lips at all times

A fair quality cross-sectional study by Naruishi et al. (2018) (SIGN evidence level 2-), identified the features of oral condition (stability of posterior occlusion as defined by normal posterior teeth or dentures) to be independently related to aspiration pneumonia. Oral condition was assessed by dentists, which may make this study difficult to replicate. Aspiration pneumonia is a multifactorial outcome measure and may not just be related to EDS difficulty (Langmore et al., 1998). The study also included patients with and without cognitive impairment, did not report results for the severity of cognitive impairment and only assessed swallowing function by videofluoroscopic swallowing study in 17% of the study population. In this small subset of the study population, a significant relationship was observed between identification of a swallowing disorder on videofluoroscopic swallowing studies and opened lips at all times. It would be easy to measure opened lips at all times, but this would be a relatively advanced sign of EDS difficulty.

### Candy sucking test

A pilot diagnostic study of the novel 'candy sucking test' showed a significant relationship with oral transit time on

videofluoroscopic swallowing studies (Mori et al., 2017). The study population by Mori et al. (2017) was not as representative of the target population of early-stage dementia (median Mini-Mental State Examination score = 10) and was at particular risk of both selection and reporting bias. The Mini-Mental State Examination score can be used as a surrogate measure for the clinical dementia rating. Scores of 11–20 have substantial agreement with moderate dementia, and 0–10 for severe dementia (Perneczky et al., 2006). In addition, the possibility of accidental swallowing or choking precludes use of the 'candy sucking test' from a risk–benefit perspective.

#### **DISCUSSION**

In this study a comprehensive range of studies related to EDS evaluation in early-stage dementia (mainly Alzheimer's disease) have been identified and reviewed. On the balance of measurability, reliability and applicability the most promising indicators of EDS difficulty include delayed oral transit (Priefer & Robbins, 1997), rinsing ability (Sato et al., 2014), sarcopenia (Özsürekci et al., 2020) and polypharmacy (Özsürekci et al., 2020). Additional less reliable and applicable indicators to be considered include opened lips at all times (Naruishi et al., 2018) and non-amnestic mild cognitive impairment in men (Yang et al., 2014). Delayed pharyngeal response (Priefer & Robbins, 1997) is subjectively measured when instrumental assessment is not available and the 'candy sucking test' (Mori et al., 2017) cannot be recommended because there is an inherent choking risk. This information could help to develop pathways to support the early identification of EDS difficulties for people living with early-stage dementia with a view to preventing complications of EDS difficulty (Gilmore-Bykovskyi and Rogus-Pulia, 2018), supporting family members/carers (Egan et al., 2020) and reducing overall healthcare consumption (Paranji et al., 2017).

More reliable and clinically measurable indicators of EDS difficulty are needed to help develop pathways to support diagnosis, and previous reviews of this area require updating with a specific focus on indicators of EDS difficulty (Affoo et al., 2013; Alagiakrishnan et al., 2013). In the scoping review by Affoo et al. (2013) evidence was identified that EDS difficulty, as well as autonomic nervous system dysfunction may occur in Alzheimer's disease. In the systematic review by Alagiakrishnan et al. (2013) it was identified that EDS difficulty developed during the late stages of frontotemporal dementia, but it was seen during the early stage of Alzheimer's disease.

The indicators of EDS difficulty in early-stage dementia identified by this updated review are diverse, and it



is unclear if the EDS indicators highlighted are merely associated with EDS difficulty or if they are also causative factors. Certain indicators of EDS difficulty reported in the literature are also medical in nature (e.g., sarcopenia and polypharmacy), and less likely to be reported by a service user. Delayed oral transit and poor rinsing ability are more directly linked and physiologically associated indicators of EDS difficulty that we speculate could be more readily reported by a service user. There was a lack of studies identified on indicators of EDS difficulty from the perspective of people living with dementia or their carers.

Priefer and Robbins (1997) reported delayed oral transit and delayed pharyngeal response as potential indicators of EDS difficulty in early-stage dementia, with measurements taken during videofluoroscopic swallowing studies. In a study by Branco et al. (2019) of people with Parkinson's disease, a more useful and clinically applicable definition of delayed oral transit is provided (over 4 s). This definition could be incorporated into identification of EDS difficulty in early-stage dementia. Unfortunately, a clinical definition for reduced larynx elevation, which was another part of the assessment used by Branco et al. (2019) was not provided in the study. This would have been of interest given that reduced hyolaryngeal elevation on videofluoroscopic swallowing studies has been observed in patients with early Alzheimer's disease. Although these observations were made in the supine rather than upright position in a functional magnetic resonance imaging study of swallowing. The applicability of this observation is limited and was a reason for excluding (at the full text assessment stage) the study that reported this observation (Humbert et al., 2010).

In cognitive impairment, two different approaches were identified for the detection of EDS difficulty and included assessment of oral condition and evaluation of executive function (Naruishi et al., 2018; Yang et al., 2014). One of the main findings was that the coexistence of cognitive impairment with oral frailty was found to significantly increase the risk of aspiration pneumonia. The risk of aspiration pneumonia was even higher when cerebrovascular disease was also present (Naruishi et al., 2018). A significant relationship was also observed between identification of a swallowing disorder on videofluoroscopic swallowing studies and opened lips at all times. No mechanism for this finding was reported by Naruishi et al., but opened lips at all times would be an advanced sign of EDS difficulty, consistent with poor oro-motor function. A further finding was that men with non-amnestic cognitive impairment, which is associated with a poorer level of executive function, as opposed to amnesic mild cognitive impairment, are more likely to have EDS difficulty on a Standardized Swallowing Assessment. Neither type of mild cognitive impairment was related to EDS difficulty in women (Yang et al., 2014).

Patients with dementia frequently suffer reduced salivary secretions, poor oral health and bacterial overgrowth (Rogus-Pulia et al., 2015). In a study of oral condition, mild cognitive impairment patients exhibited significantly more tooth staining and poorer performance on repetitive saliva swallow test (Takahashi et al., 2019). In dentulous nursing home residents, there was a significant association between preserved cognitive function and a reduced risk of EDS difficulty on water swallow test. Although a similar relationship was not identified in the edentulous participants, edentulous individuals with cerebrovascular disease had an increased risk of EDS difficulty. This highlights cerebrovascular disease as a potential important confounding factor in this study and again emphasises cerebrovascular disease as an important risk factor for EDS difficulty in the cognitively impaired client group (Yatabe et al., 2018). Two studies assessing the relationship of oral function with EDS difficulty in patients with cognitive impairment have also emphasised the importance of coexisting cerebrovascular disease (Naruishi et al., 2018; Yatabe et al., 2018). In keeping with this observation, a further study in individuals with Alzheimer's disease identified the presence of silent brainstem infarction as a significant independent predictor of aspiration pneumonia (Wada et al., 2001). This observation is similar to the independent relationship between brainstem impairment and EDS difficulty in multiple sclerosis, further underpinning the importance of brainstem control of safe and effective swallowing (Calcagno et al., 2002).

Other clinical factors associated with EDS difficulty in the Alzheimer's group included sarcopenia and polypharmacy (Özsürekci et al., 2020). In a reverse of this analysis, another study identified in the search reported that an independent relationship existed between poor swallowing function on modified water swallow test and decreased skeletal muscle index (Takagi et al., 2017). This study assessed for indicators of decreased skeletal muscle as opposed to indicators of EDS difficulty (so was excluded at the full text review stage), but it does show that the reverse relationship exists (Takagi et al., 2017). However, no relationship was identified between nutritional status and EDS difficulty in another study patients that was also excluded at the full text assessment stage (Goes et al., 2014). The authors of this study discussed that this small study of 30 patients was contrary to other evidence, and in their study the process of malnutrition was slower to evolve than the EDS difficulty. This collective evidence suggests that it is worth exploring further the relationship between sarcopenia and nutrition with EDS difficulty, but the timing of EDS assessment is critical when considering whether there is definite association.

Consistent with importance of polypharmacy there was a significant association identified between aspiration

TABLE 2 Summary of studies included in previous review from Affoo et al. (2013)

Study	Study description	Oxford Centre for Evidence-Based Medicine Level of evidence	Conclusion
Humbert et al.  (2010)  Described or characterized dysphagia in Alzheimer's of through comparison of two more groups		Not assigned	Dysphagia occurs early in Alzheimer's disease Dysphagia in early Alzheimer's disease may be associated with functional change of the cortical swallowing network
Humbert et al. (2010)	Described or characterized dysphagia in Alzheimer's disease through a comparison of two or more groups	Not assigned	Dysphagia occurs early in Alzheimer's disease Dysphagia in early Alzheimer's disease may be associated with functional change of the cortical swallowing network
Priefer and Robbins (1997)	Described or characterized dysphagia in Alzheimer's disease through comparison of two or more groups	Not assigned	Dysphagia occurs early in Alzheimer's disease Dysphagia occurs in the oral and pharyngeal stages of swallowing
Horner et al. (1994)	Prospective case series	4	Dysphagia occurs in the oral and pharyngeal stages of swallowing Disease severity may be associated with dysphagia severity
Suh et al. (2009)	Described or characterized dysphagia in Alzheimer's disease through comparison of two or more groups	Not assigned	Dysphagia occurs in the oral and pharyngeal stages of swallowing
Wada et al. (2001)	Described or characterized dysphagia in Alzheimer's disease through comparison of two or more groups	Not assigned	Dysphagia in the oral and pharyngeal stages of swallowing Disease severity may be associated with dysphagia severity

pneumonia and neuroleptic use in the Alzheimer's disease population (Wada et al., 2001). The use of antiepileptic drugs that have sedative properties are also independently associated pneumonia risk in community-based individuals with Alzheimer's disease (Taipale et al., 2019). When specifically assessing the impact of antipsychotic medications, a study identified in the systematic search reported that on videofluoroscopic swallowing studies there were no differences in the penetration aspiration scale or laryngeal vestibule closure time in patients with dementia that were taking and not taking antipsychotic medications (Miarons et al., 2018).

# Importance, strengths and limitations

A strength of this review is the systematic approach taken, which was required given the heterogeneous nature of

the study populations. Mild cognitive impairment can be considered a prodromal phase between healthy aging and Alzheimer's dementia (Winchester & Winchester, 2016). However, a diagnosis of mild cognitive impairment is distinct from dementia and may be a precursor other diseases such as cerebrovascular disease (Knopman & Petersen, 2014). The severity of dementia can be classified according to a clinical dementia rating scale and mild cognitive impairment is consistent with a clinical dementia rating scale of 0.5 (Takahashi et al., 2019). In some previous studies that have aimed to recruit individuals with 'early-stage' dementia, inclusion criteria are variable and have included a clinical dementia rating of 0.5-1 (Boots et al., 2018), a clinical dementia rating of 0.5-1 or a formal diagnosis of early-stage dementia (by general practitioner or specialist) (Stockwell-Smith et al., 2019), a clinical dementia rating no greater than 1 (McGee et al., 2017), or mild to moderate cognitive impairment (as determined by a Mini-Mental

Summary of studies included in previous review by Alagiakrishnan et al. (2013) TABLE 3

Evidence level	В	м	В	В	В
Conclusions/outcomes	Alzheimer's disease patients had prolonged oral transit duration for solids, pharyngeal response for liquids and total swallow duration for liquids, received more cueing or assistance by caregiver	Alzheimer's disease patients had reduced mean extent of hyoid movement and mean extent of laryngeal elevation	Severe Alzheimer's patients had worse oral praxis score and global video fluoroscopic score	Vascular dementia patients had significant difficulty in bolus formation and mastication and had significantly increased risk of silent aspiration Alzheimer's disease patients had a significant oral transit delay of well over 5 s	Difference between Alzheimer's disease and fronto-temporal dementia in the overall frequency of abnormal eating behaviours in different domains and it was higher in fronto-temporal dementia, except for swallowing problems which is higher in Alzheimer's disease
Type of assessment	Clinical swallow evaluation Videofluoroscopic swallowing studies	Videofluoroscopic swallowing studies	Clinical swallow evaluation Videofluoroscopic swallowing studies	Videofluoroscopic swallowing studies	Clinical swallow evaluation
Subjects and assessment method	<ul> <li>N = 10 Alzheimer's disease (mild as defined by clinical dementia rating scale)</li> <li>N = 13 (controls)</li> <li>Mean age = 68</li> <li>Observed patients and controls have a meal</li> </ul>	<ul> <li>N = 24 (13 mild Alzheimer's disease, mean Mini-Mental State</li> <li>Examination score = 23) functional magnetic resonance imaging BOLD</li> </ul>	N = 25, 56% female Mean age = 74 Mini-Mental State Examination score 10–20 in moderate and 1–10 in severe (mean 13.24) Caregiver questionnaire	N = 49 38% female Mean age = 73 years	N = 91 37% female Mean age = 65 years Mini-Mental State Examination score mean = 20.2 Questionnaire evaluating five domains: swallowing problems, appetite change, food preference, eating habits, other oral behaviour
Prevalence	32%	Not provided	Moderate 28.6% Severe 44%	Alzheimer's disease 13% Vascular dementia 47%	Fronto-temporal dementia 26% Alzheimer's disease 7%
Design	Prospective case-controlled study	Case-control study	Prospective cohort study	Retrospective cohort study	Survey
Study	Priefer and Robbins (1997)	Humbert et al. (2010)	Horner et al. (1994)	Suh et al. (2009)	(2002)

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State Examination score  $\geq$  18 points) (Clare et al., 2019). The lack of consensus with regards to defining early-stage dementia contributes to the heterogeneity of the published literature. In the area of early-stage dementia research there is a need for uniformity of clinical definitions and more robust studies on indicators of EDS difficulty. It is interesting to note the absence of previous episodes of EDS difficulty as Scharitzer et al. (2017) have highlighted the importance of taking a full patient history in order to identify prior or first-episode swallowing difficulties. History-taking is often implicit in the process of implementation of clinical indicators, but prior episodes may also be important to consider in any listing of indicators or predictors.

The search used in this systematic review has identified all studies included in previous reviews (Affoo et al., 2013; Alagiakrishnan et al., 2013). Therefore, the search strategy was validated. In a previous scoping review of swallowing in Alzheimer's disease by Affoo et al. (2013) a summary of clinical studies using instrumental assessment of swallowing in Alzheimer's disease identified similar studies to this systematic review. The evidence level of studies identified by Affoo et al. was classified using the Oxford Centre for Evidence-Based Medicine Levels of Evidence (Table 2). However, when using the Oxford Centre for Evidence-Based Medicine levels of Evidence many of the studies were not assigned a particular evidence level by Affoo et al. In a systematic review of swallowing in dementia by Alagiakrishnan et al. (2013), similar studies were identified to Affoo et al. (2013), and the levels of evidence were graded according to the Agency for Healthcare Research and Quality Interpretation (Table 3). This current review has updated the previous reviews with more recently published studies (Mori et al., 2017; Naruishi et al., 2018; Özsürekci et al., 2020; Sato et al., 2014; Yang et al., 2014) and has had a much greater focus on discovering indicators of EDS difficulty. The use of multiple different critical appraisal tools was necessary due to the different study designs. An appropriate tool was therefore used for each study, but comparability of study assessment scores was reduced as result. An alternative approach could have been to modify a single critical appraisal tool to be used for all studies. Despite using different tools, it was possible to classify the evidence level in a uniform way using the Scottish Intercollegiate Guidelines Network grading system (SIGN, 2015).

#### **CONCLUSIONS**

There remains a lack of consistency in the approach to identifying EDS difficulty in early-stage dementia. There is a relative paucity of studies reporting indicators of EDS difficulty for people with early-stage dementia in the published literature. The indicators of EDS difficulty in early-stage dementia reported in the literature are diverse. EDS difficulty in early-stage dementia is associated with delayed oral transit, poor rinsing ability, as well as presence of sarcopenia and polypharmacy. These indicators of EDS difficulty could help to initiate pathways to support the early identification of EDS difficulties for people living with early-stage dementia. This could allow for discussions to take place at an earlier stage to establish the wishes of individuals if EDS difficulties progress further. Shared decisions could therefore be discussed at a time when the cognitive abilities of the person living with dementia are maintained, and their individual wishes can be personally communicated to family or carers. However, the evidence would be incomplete without eliciting the experiences of people living with dementia, their families' perspectives and professional opinion on potential indicators of EDS difficulty. There is a need for further studies to explore indicators of EDS difficulty from the perspective of people living with dementia and carers.

#### DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

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#### APPENDIX A

#### SEARCH TERMS

- 1. Deglutition Disorders/
  - 2. (dysphagia or swallow\* or deglut\*)
  - 3.1 or 2
  - 4. indicat\*
  - 5. detect\* or identif\* or sign\* or behavio?r or predict\*)
  - 5. 4 or 5
  - 7. Cognitive Dysfunction/

- 8. dementia/ or alzheimer disease/
- 9. (MCI or mild cognitive impairment or alzheimer\* or dementia)
  - 10. 7 or 8 or 9
  - 11. 3 and 6 and 10
  - 12. Deglutition Disorders/
  - 13. (dysphagia or swallow\* or deglut\*)
  - 14. 12 or 13
  - 15. indicat\*

- 16. (detect\* or identif\* or sign\* or behavio?r or predict\*)
  - 17. 15 or 16
  - 18. Cognitive Dysfunction/
  - 19. dementia/ or alzheimer disease/
- 20. (MCI or mild cognitive impairment or alzheimer\* or dementia)
  - 21. 18 or 19 or 20
  - 22. 14 and 17 and 21