Outcome Measurement in the Treatment of Spasmodic Dysphonia: A Systematic Review of the Literature

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Summary: Purpose. The aim of this review was to systematically identify all available studies reporting outcomes measures to assess treatment outcomes for people with spasmodic dysphonia (SD).

Methods. Full-text journal articles were identified through searches of PubMed, Embase, CINAHL, and Cochrane databases and hand searching of journals.

Results. A total of 4,714 articles were retrieved from searching databases; 1,165 were duplicates. Titles and abstracts of 3,549 were screened, with 171 being selected for full-text review. During full-text review, 101 articles were deemed suitable for inclusion. An additional 24 articles were identified as suitable for inclusion through a hand search of reference lists. Data were extracted from 125 studies. A total of 220 outcome measures were identified. Considered in reference to the World Health Organization International Classification of Functioning, Disability and Health (ICF), the majority of outcomes were measured at a Body Function level (n = 212, 96%). Outcomes that explored communication and participation in everyday life and attitudes toward communication (ie, activity and participation domains) were infrequent (n = 8; 4%). Quality of life, a construct not measured within the ICF, was also captured by four outcome measures. No instruments evaluating communication partners' perspectives or burden/disability were identified.

Conclusions. The outcome measures used in SD treatment studies are many and varied. The outcome measures identified predominately measure constructs within the Body Functions component of the ICF. In order to facilitate data synthesis across trials, the development of a core outcome set is recommended.

Key Words: Spasmodic dysphonia−Laryngeal dystonia−Treatment outcomes−Outcome measures−Systematic review.

INTRODUCTION

Spasmodic dysphonia (SD) is a task-specific focal dystonia of the larynx. SD comprises two major clinical forms: adductor (AD) and abductor (AB) SD. AD SD is characterized by an effortful, strained, or strangled voice quality with irregular, abrupt, or intermittent voice stoppages (breaks) associated with inappropriate adduction of the vocal folds[1] during speech. AD SD accounts for approximately 80% of all cases of SD.[2] AB SD is less common and is characterized by breathiness, pitch alterations, and phonatory breaks as a result of uncontrollable vocal fold opening, especially during the production of voiceless consonants.[1] SD is estimated to affect approximately 50,000 people in North America,[3] with the disorder affecting women more often than men.[4] The onset of SD, most common in the fourth or fifth decade of life, is usually gradual with no known precipitating cause.[5] Symptoms generally worsen over an 18-month period and then remain stable in severity from that point onward.[5] SD is a chronic debilitating condition that often extends beyond the impairment of vocal communication and causes significant restrictions and limitations that negatively affect social, professional, economic, and psychological functions of daily living.[6,7] SD becomes even more incapacitating when it is associated with dystonic (focal, action induced) vocal tremor (VT), which is present in 25%−30% of patients with SD and is characterized by rhythmic alterations in pitch and loudness during vowel production and the inability to sustain a vowel for more than a few seconds.[8,9] The presence of VT often complicates the diagnosis and clinical management of SD and may be associated with poorer treatment outcomes.[4,10,11]

The current gold standard and most widely employed treatment of SD ± VT is directed toward the temporary improvement of voice symptoms with repeated injections of botulinum toxin into the laryngeal musculature every 3−4 months for life.[10] However, this is not effective in all SD patients and is even less effective in combined SD/VT cases.[12] The maximum treatment-related benefits usually last for only about 30% of each injection cycle and may be accompanied by side effects in over 50% of patients.[12] As such, other treatment options, including pharmacological and surgical interventions, have also been explored but are not well established.

In order to delineate the optimal treatment approach, it is important to be able to compare outcomes (end points or results) of different treatment modalities. In treatment research, a primary outcome is selected to draw conclusions regarding the overall effectiveness of an intervention.[13] The choice of an outcome and an instrument with which to measure it is crucial to the success of a research study. Poorly chosen outcomes and outcome instruments may be unable to capture, or may even distort, research results.[14] In the field of SD research, where sample sizes are typically small, the heterogeneity in outcome measurement and the tools with which outcomes are measured limit opportunities to amass treatment evidence across trials.

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In order to produce compatible data that can be easily synthesized across trials, researchers have proposed the development and use of core outcome sets (COSs). The use of a COS does not limit the number of outcomes able to be evaluated but rather represents the minimum set of outcomes that should be measured and reported in research trials.[15,16] The use of a COS may (1) assist research designers to select the most appropriate and best-quality tools for measuring a given outcome construct; (2) provide minimum standards of reporting research findings, increasing research transparency, and reliability; (3) produce data that are compatible across studies, enabling efficient synthesis for future analysis (eg, systematic reviews); and (4) target outcomes relevant to end users, which will be more likely to inform treatment decision making. Consensus-based guidelines for the selection of outcome measurement instruments for the outcomes included in a COS have recently been published.[17] The authors outline four steps that should be undertaken in this process: (1) consideration of constructs to be measured; (2) finding existing outcome measures; (3) quality assessment of outcome instruments; and (4) selection of outcome instruments using a final consensus procedure. This study reflects step 2 in the above process. To the authors' knowledge, no previous studies have sought to broadly identify and review outcome instruments used in the treatment of people with SD, irrespective of the construct measured. Therefore, the aim of the current systematic review was to identify all available studies reporting effects of treatment in the SD population and examine the outcome measurement tools used. Through the systematic identification of these studies, the authors sought to identify (1) which outcome measurement instruments have been used to measure the effects of treatment in SD and (2) what constructs are measured by these instruments.

METHODS

Protocol, registration, and data management

The protocol for this systematic review was registered on PROSPERO (2017: CRD42017059839) at http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017059839.

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[18]

Primary searches (from inception to March 2017) were run using PubMed, Embase, CINAHL, and Cochrane Library databases on April 13, 2017. The full electronic search strategy for all databases is available in Table 1. Reference lists from identified articles were hand-searched to find further potentially eligible articles between May and August 2017. The initial search incorporated no filters to ensure the majority of relevant studies were captured.

Studies sourced from the electronic databases were imported into *Endnote* (Clarivate Analytics, Philadelphia, USA; endnote.com), where duplicates were excluded. Title and abstract screening and full-text review were conducted using *Covidence* systematic review software (Veritas Health Innovation, Melbourne, Australia) (available at www.covidence.org). Data extraction was managed using Microsoft Office Excel (Microsoft Corporation, Washington, USA).

Study selection

Two reviewers (AR and PA) independently screened titles and abstracts for eligibility for inclusion using predefined inclusion and exclusion criteria. The following study inclusion criteria were applied:

(a) adult participants (18+ years of age) with a diagnosis of SD (AD, AB, or mixed) with or without concomitant VT, confirmed by otolaryngology and/or neurology;
(b) studies with pretreatment and post-treatment objective, subjective or quality-of-life outcome data, including those reported by proxies of people with SD (ie, caregiver/significant others or health professionals);
(c) studies reported in full-text journal articles; and
(d) studies reported in English.

Systematic reviews, literature reviews, animal studies, editorials, conference abstracts, and opinion papers were excluded. Furthermore, treatment studies that reported posttreatment effects with no explicit and/or discrete measurement of pretreatment status were excluded.

Two independent reviewers (AR and PA) screened selected full-text articles. The reference lists of included articles were hand-searched to find all other potentially eligible articles. A third reviewer (DN) was available to make a decision regarding the inclusion of articles in the case of disagreement between the two reviewers. Final selection was based on the full consensus of all reviewers. Figure 1 presents an overview of the study selection process.

Data extraction

One author (AR) independently extracted descriptive data regarding study design, study population, intervention, outcomes, and assessment intervals. The outcome measures included objective voice assessment (eg, acoustic analysis), subjective voice assessment (patient or clinician rated), and quality-of-life assessment (patient or clinician rated). To ensure interrater reliability, data extraction was repeated for 10% of all included articles by an independent author (PA).

RESULTS

Search and selection

A total of 4,714 articles were retrieved from searching databases; 1,165 were duplicates. Titles and abstracts of 3,549 were screened, with 171 being selected for a full-text review. During the full-text review, 101 articles were deemed suitable for inclusion. An additional 24 articles were identified as suitable for inclusion via hand searching of reference lists. Data were extracted from 125 studies. A summary of characteristics for all included studies is presented in Table 2.

TABLE 1.
Search Strategy

PubMed (1591)	((((((((("Botulinum Toxins"[Mesh]) OR "onabotulinumtoxinA"[Supplementary Concept]) OR ("denervation reinnervation" OR DeRe[tiab])) OR "thyroarytenoid myectomy") OR "medialization laryngoplasty") OR (botox[tiab] OR "botulinum toxin"[tiab] OR "botulinum toxins"[tiab] OR botulin*[tiab])) OR ("sodium oxybate"[tiab] OR xyrem[tiab]))) AND ((((((((((tremor[tiab] AND (voice[tiab] OR vocal[tiab] OR phonat*[tiab]))) OR (abductor[tiab] AND (spasm*[tiab] OR dysphon*[tiab]))) OR (adductor[tiab] AND (spasm*[tiab] OR dysphon*[tiab]))) OR (ADSD[tiab] AND voice[tiab])) OR (ABSD[tiab] AND voice[tiab])) OR "spastic dysphonia"[tiab]) OR "laryngeal dystonia"[tiab]) OR "spasmodic dysphonia"[tiab]) OR (((((("Voice Disorders"[Mesh]) OR "Dysphonia"[Mesh]) OR "Laryngeal Diseases"[Mesh]) OR "Laryngismus"[Mesh]) OR "Dystonia"[Mesh]))) AND (treatment OR management OR intervention OR rehabilitation)
Cochrane (17)	#1MeSH descriptor: [Dysphonia] explode all trees #2MeSH descriptor: [Voice Disorders] explode all trees #3MeSH descriptor: [Laryngeal Diseases] explode all trees #4MeSH descriptor: [Laryngismus] explode all trees #5 MeSH descriptor: [Dystonia] explode all trees #6"spasmodic dysphonia":ti,ab,kw (Word variations have been searched) #7 "laryngeal dystonia":ti,ab,kw (Word variations have been searched) #8 "spastic dysphonia":ti,ab,kw (Word variations have been searched) #9 "ABSD" and voice:ti,ab,kw (Word variations have been searched) #10 "ADSD" and voice:ti,ab,kw (Word variations have been searched) #11 tremor near voice or vocal or phonat*:ti,ab,kw (Word variations have been searched) #12 {or #1-#5} #13 {or #6-#11} #14 {and #12-#13} #15 MeSH descriptor: [Botulinum Toxins] explode all trees #16 "denervation reinnervation":ti,ab,kw (Word variations have been searched) #17 "thyroarytenoid myectomy":ti,ab,kw (Word variations have been searched) #18"medialization thyroplasty":ti,ab,kw (Word variations have been searched) #19botox or botulin*:ti,ab,kw (Word variations have been searched) #20 "sodium oxybate" or xyrem:ti,ab,kw (Word variations have been searched) #21 {or #16-#20} #22 {and #15, #21} #23 {and #14, #22}
Embase (2785)	● #1 "dysphonia"/exp OR "spasmodic dysphonia"/exp OR "voice disorder"/exp OR "larynx disorder"/exp OR "larynx spasm"/exp OR "dystonia"/exp ● #2 "spasmodic dysphonia":ti,ab ● #3 "laryngeal dystonia":ti,ab ● #4 "spastic dysphonia":ti,ab ● #5 "absd":ti,ab AND voice:ti,ab ● #6 "adsd":ti,ab AND voice:ti,ab ● #7 "adductor":ti,ab AND spasm*:ti,ab ● #8 "abductor":ti,ab AND spasm*:ti,ab ● #9 "abductor":ti,ab AND dysphon*:ti,ab ● #10 "adductor":ti,ab AND dysphon*:ti,ab ● #11 "tremor":ti,ab AND (voice:ti,ab OR vocal:ti,ab OR phonat*:ti,ab) ● #12 {#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11} ● #13 "botulinum toxin"/exp OR "botulinum toxin a"/exp ● #14 "denervation reinnervation" OR "dere" ● #15 "thyroarytenoid myectomy" ● #16 "medialization laryngoplasty" ● #17 botox:ti,ab OR botulin*:ti,ab ● #18 "sodium oxybate" OR xyrem ● #19 "sodium oxybate" OR "oxybate sodium" ● #20 {#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19} ● #21 {#12 AND #20} ● #22 treatment OR management OR intervention OR rehabilitation ● #23 {#21 AND #22}
CINAHL (321)	S1: MH "Voice Disorders" S2: MH "Dysphonia, Spasmodic" S3: MH "Laryngeal Diseases" S4: MH "Dystonia" OR MH "Dystonic Disorders" S5: "Spasmodic dysphonia" S6: "laryngeal dystonia" S7: "spastic dysphonia" S8: "ABSD" AND "voice" S9: "ADSD" AND "voice" S10: "adductor N2 spasm*" OR "adductor N2 dysphon*" S11: "abductor N2 spasm*" OR "abductor N2 dysphon*" S12: "tremor N5 voice" OR "temor N5 vocal" OR "tremor N5 phonat*" S13: "laryngismus" S14: S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 S15: MH "Botulinum Toxins" S16: "denervation reinnervation" OR "Dere" S17: "thyroarytenoid myectomy" S18: "medialization laryngoplasty" S19: "botox" OR "botulin*" S20: "sodium oxybate" OR "xyrem" S21: S15 OR S16 OR S17 OR S18 OR S19 OR S20 S22: S14 AND S21

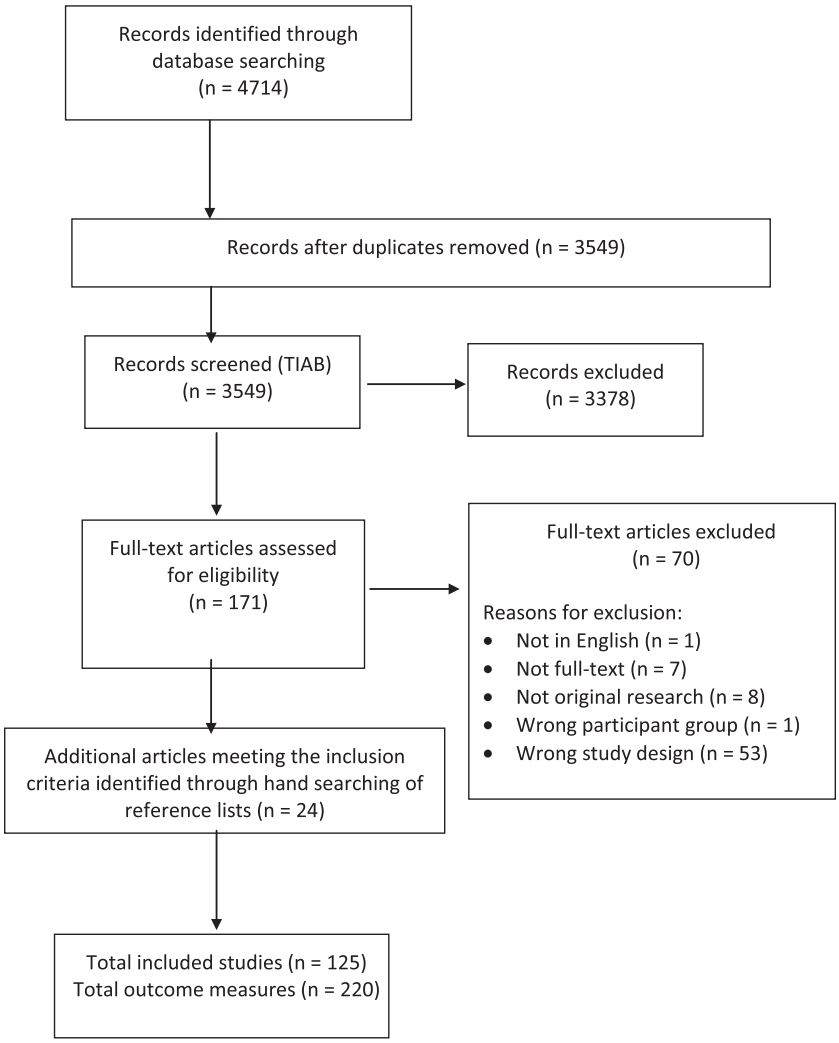

FIGURE 1. Study Selection Flowchart. TIAB, title and abstract.

Data extraction

Of the 125 included studies, the majority of studies (n = 88, 70.4%) examined the effects of botulinum toxin injections on AD SD (n = 80/88, 90.0%), AB SD (n = 14/88, 15.9%), and mixed SD (n = 4/88, 4.5%) (see Table 2). For one study examining the effect of botulinum toxin treatment, the type of SD was undisclosed.[129] The effectiveness of botulinum toxin injections alone and botulinum toxin injections with the addition of voiced therapy for individuals with AD SD was compared in a further two studies.[98,116] An additional 31 studies evaluated the effect of various surgical treatments on AD SD, including recurrent laryngeal nerve resection (n = 9[27,28,51,52,63,64,74,121,130];), myotomy or myectomy (n = 10[65,72,80,81,99,100,119,120,124,125]), myoplasty or thyroplasty (n = 7[46,73,100,110–112,115]), selective laryngeal adductor denervation-reinnervation (n = 3[25,32,47]), radiofrequency thyroarytenoid myothermy (n = 2[77,103]), and autologous replacement of the vocal fold (n = 1[126]). Two studies explored the use of sodium oxybate +/− botulinum toxin in SD with or without concomitant VT.[108,117] The remaining three studies explored the use of a range of behavioral or alternative therapies for the treatment of AD SD including acupuncture,[49] electromyography (EMG) biofeedback in conjunction with progressive relaxation exercises,[70] and a 3-week stutter-free speech program.[93]

Identified outcome instruments

For the purpose of this study, a single method by which pre-post data were analyzed and reported (eg, mean fundamental frequency) was counted as an individual outcome instrument. Outcome instruments that were not explicitly defined and descriptive reports of outcomes, although mentioned within the following sections, have not been counted. Outcome instruments were broadly classified in two ways: (1) as objective, subjective, or related to cognitive, psychosocial-emotional, or quality-of-life domains (see Table 2) and (2) within the World Health Organization (WHO) International Classification of Functioning, Disability and Health (ICF)[142] framework.

A quality assessment for each outcome instrument has not been included as this is outside the scope of the current study. Reference to widely available outcome instruments and their

TABLE 2.
Summary of Included Studies and the Categories of Pre-Post Outcome Measures Reported

Study	Design*	Patients†	N (% Female)	INT‡	Outcome			Pre-post follow-up interval/s#
					OBJ§	SBJ‖	PSE/QOL¶	
Abdoerrachman[19]	●	●	9 (78)	●	●	●■	○	● ○ 2 months
Adams et a[20]	●	●	30 (67)	●	●	○	○	● ○ 2–4 weeks, 10–12 weeks
Adams et al[21]	●	●	26 (UD)	●	●	■	○	● ○ 2 and 6 weeks
Adams et al[22]	●	●	50 (68)	●	●	■	○	● ○ 2 and 6 weeks
Adler et al[23]	●	●	13 (69)	●	○	●■	○	● ○ 1, 4, and 8 weeks
Ali et al[24]	●	●	9 (67)	●	●	○	○	● ○ 24 +/− 4 days
Allegretto et al[25]	●	●	6 (17)	○	●	■□	○	● ○ 11–29 months (mean 20.3 months)
Anari et al[26]	●	●○□	34 (88)	●	○	○	●	● ○ 1 day, 2 weeks
Aronson and DeSanto[27]	●	●	37 (70)	○	○	●■	○	● ○ 1 day and 1, 6, 12, 18 months
Aronson and DeSanto[28]	●	●	33 (67)	○	○	●■	○	● ○ 1 day and 1, 6, 12, 18, 24, 30, 36 months
Aronson et al[29]	●	●	10 (80)	●	○	●	○	● ○ 24 and 48 hours, 2 weekly intervals until 8.5 months
Bender et al[30]	●	●	10 (90)	●	○	■□	○	● ○ 3–6 weeks
Benninger et al[31]	●	●	22 (77)	●	○	○	●	● ○ 2–4 weeks
Berke et al[32]	●	●	21 (52)	○	○	■	○	● ○ Mean 31.4 months (range = 12–68 month
Bielamowicz et al[33]	●	○	15 (80)	●	○	■	○	● ○ 2 weeks
Bielamowicz and Ludlow[34]	●	●	10 (50)	●	●	■	○	● ○ 2 weeks
Blitzer and Brin[35]	●	●○	320 (59)	●	○	●■	○	● ○ UD
Blitzer and Brin[36]	●	●○	450 (UD)	●	○	●■	○	● ○ UD
Blitzer et al[37]	●	○	32 (34)	●	○	●■	○	● ○ UD
Blitzer et al[10]	○	●○	901 (64)	●	○	●■	○	● ○ Daily for 2 weeks then weekly until next treatment
Boseley et al[38]	□	●	1 (100)	●	●	○	○	● ○ UD
Brin et al[39]	●	●	42 (50)	●	○	●	○	● ○ 3 days, 2 weeks
Brin et al[40]	○	●○	901 (64)	●	○	●	○	● ○ UD
Cannito et al[41]	○	●	16 (100)	●	●	■	○	● 2 weeks ○ 3–6 weeks
Cannito et al[42]	●	●	42 (86)	●	●	■	○	● Within 2 weeks ○ 3–6 weeks
Cannito et al[43]	●	●	20 (80)	●	○	○	●	● ○ 1 week, 2 months
Cannito et al[44]	●	●	42 (86)	●	○	■	○	● Within 2 weeks ○ 2–6 weeks
Cantarella et al[45]	●	●	24 (79)	●	●	○	○	● ○ Mean 14.4 days (range = 8–20 days)
Chan et al[46]	●	●	13 (62)	○	○	●	○	● ○ <3 months, 3–6 months, >12 months
Chhetri et al[47]	●	●	83 (72)	○	○	■	○	● ○ Mean 49 months
Courey et al[48]	●	●	38 (79)	●	○	○	●	● ○ 1 month
Crevier-Buchman et al[49]	□	●	2 (0)	●/□	●	○	○	● 1 or 2 months ○ 3 or 6 months
Damrose et al[50]	●	●○	102 (75)	●	○	■	○	● ○ 6 weeks, immediately before second treatment (~12 months + after first treatment), 6 weeks after second treatment, immediately before third treatment (~12 months + after third treatment), 6 weeks after third treatment

(*Continued*)

TABLE 2. (*Continued*)

Study	Design*	Patients†	N (% Female)	INT‡	Outcome			Pre-post follow-up interval/s#
					OBJ§	SBJ‖	PSE/QOL¶	
Dedo and Behlau[51]	●	●	300 (UD)	○	●	■	○	● ○ 5–14 years
Dedo and Izdebski[52]	○	●	28 (UD)	○	○	■	○	● ○ 1–5 years
Dejonckere et al[53]	UC	●	12 (UD)	●	●	■	●	● immediately prior ○ a few weeks
Dromey et al[54]	●	●	7 (57)	●	●	□	○	● Within 1 week ○ 4–6 weeks
Epstein et al[55]	●	●	40 (58)	●	○	■	●	● 1 day, 2 hours ○ immediately post, 1 week
Epstein et al[56]	●	●	40 (58)	●	○	■	●	● 1 day, 2 hours ○ immediately post, 1 week
Esposito et al[57]	●	●	13 (UD)	●	●	○	●	● ○ 2 weeks after for 4 consecutive treatments performed every 5 months
Finnegan et al[58]	●	●, ●■	5 (80)	●	●	○	○	● ○ 2, 4, 8 weeks
Fisher et al[59]	□	●	1 (0)	●	●	■	○	● ○ 1 hour, and weekly for week 1–5 and 8–10
Fisher et al[60]	●	●	5 (40)	●	●	■	○	● ○1 hour, and weekly or bi-weekly over 8 weeks
Ford et al[61]	●	●	16 (75)	●	●	●■	○	● ○ UD
Ford et al[62]	●	●○□	58 (45; 35 UD)	●	●	●■	○	● ○ ~1 month
Fritzell et al[63]	●	●	4 (75)	○	●	○	○	● ○ UD
Fritzell et al[64]	●	●	11 (82)	○	●	■	○	● ○ 1–2 days, 5–34 months after operation, and 2–11 months after reoperation if completed
Gandhi et al[65]	●	●	15 (47)	○	○	■	●	● ○ 12, 24, and 28 months
Geneid et al[66]	●	●	17 (35)	●	○	■	●	● ○ 2 years and 11 years after discontinuation of treatment
Green et al[67]	●	●	13 (62)	●	●	○	○	● ○ UD
Hartmann et al[68]	●	●	17 (76)	●	●	■	●	● ○ 4–8 weeks
Haslinger et al[69]	●	●	12 (42)	●	●	○	○	● 6.9 +/- 7.2 months ○ 47.4 +/- 18.6 days
Henschen and Burton[70]	□	●	2 (50)	□	●	○	○	● ○ UD
Hogikyan et al[71]	●	●	27 (85)	●	○	●	●	● ○ 6–8 weeks
Hussain and Shakeel[72]	□	●	4 (50)	○	○	○	●	● ○ 2.5 years
Isshiki et al[73]	□	●	1 (100)	○	●	■	○	● ○ 17 months
Izdebski et al[74]	●	●	65 (66)	○	○	■	○	● ○ 1 year, 1–2 years, 3 + years
Kaszás et al[75]	□	●	1 (0)	●	●	■	○	● ○ UD
Kendall and Leonard[76]	●	●■	15 (UD)	●	●	■	○	● ○ ~4 weeks
Kim et al[77]	●	●	20 (100)	○	●	■	●	● ○ 2, 6, and 12 months
Kim et al[78]	●	●	30 (UD)	●	●	●	●	● ○ 1, 3, and 6 months
Klein et al[79]	●	○	14 (64)	●	○	○	●	● ○ Mean 36 days (range = 21–45 days)
Koufman[80]	□	○	4 (100)	○	○	■	○	● ○ 15, 17, 21 months
Koufman et al[81]	○	●	5 (60)	○	●	■	●	● ○ 5–19 months
Langeveld et al[82]	●	●	27 (74)	●	○	●	○	● ○ Daily for 7 days, weekly for 3 months
Langeveld et al[83]	●	●	46 (70)	●	○	●■	●	● ○ 1 month

(*Continued*)

TABLE 2. (*Continued*)

Study	Design*	Patients†	N (% Female)	INT‡	Outcome			Pre-post follow-up interval/s#
					OBJ§	SBJ‖	PSE/QOL¶	
Langeveld et al[84]	●	●	46 (70)	●	●	●■	○	● ○ When patients judged their voices to be optimal
Liu et al[85]	●	●	31 (97)	●	○	●	○	● 1 week ○ daily for 6 weeks
Liu et al[86]	●	●, ●■	10 (80)	●	○	○	●	● ○ 1 month
Ludlow et al[87]	●	●	5 (80)	●	●	○	○	● ○ 2 weeks, 4 months
Ludlow et al[88]	●	●	16 (94)	●	●	○	○	● ○ 2 weeks
Ludlow et al[89]	●	○	10 (60)	●	●	○	○	● ○ 2 weeks
Lundy et al[90]	●	●	68 (69)	●	○	●	○	● ○ Daily for 7 days, then weekly until next injection
Maronian et al[91]	○	●■	81 (86)	●	●	●	○	● ○ Before next injection
Mehta et al[92]	●	●	91 (77)	●	●	○	○	● ○ 6 weeks, immediately before second treatment (~12 months + after first treatment), 6 weeks after second treatment, immediately before third treatment (~12 months + after third treatment), 6 weeks after third treatment
Meyers and Anderson[93]	□	●	1 (0)	□	●	■	○	● Over 2 days immediately prior ○ over 2 days immediately after completion of 3-week therapy block
Miller et al[94]	□	●	1 (0)	●	●	○	○	● ○ UD
Morzaria and Damrose[95]	●	●	37 (70)	●	○	○	●	● ○ Middle third of injection cycle
Morzaria and Damrose[96]	●	●	37 (70)	●	○	○	●	● ○ Middle third of injection cycle
Murry et al[97]	●	●○□	32 (78)	●	○	○	●	● ○ 1 week, 2 months
Murry and Woodson[98]	●	●	27 (85)	●/●+□	●	○	○	● ○ 2–3 weeks
Nakamura et al[99]	●	●	7 (86)	○	○	■	○	● ○ 1 week, 1–2 months, ~6 months
Nomoto et al[100]	○	●	65 (88)	○	○	■	●	● ○ 6 + months
Novakovic et al[12]	●	●	133 (72)	●	○	●	●	● ○ Best point during the injection cycle
Paniello et al[101]	●	●	22 (86)	●	○	○	●	● ○ 2 days, 5–7 days, 2 weeks, then every 4 weeks through until end of injection cycle
Paniello et al[102]	●	●	9 (89)	●	○	○	●	● ○ 2 days, 5–7 days, 2 weeks, then every 4 weeks through until end of injection cycle
Remacle et al[103]	□	●	3 (67)	○	○	○	●	● ○ 1 month
Rhew et al[104]	●	●	12 (67)	●	●	●	○	● ○ 2–3 weeks
Rojas et al[105]	●	●	16 (69)	●	●	■	●	● ○ Mean 36 days (range = 28–49 days), and mean 137 days (range = 112–189 days)
Rontal et al[106]	●	○	6 (50)	●	●	■	○	● ○ UD
Rubin et al[107]	●	●	42 (85)	●	○	●	●	● ○ 6–8 weeks
Rumbach et al[108]	●	●○, ●■, ○■	50 (74)	■/■+●	○	●■	○	● ○ 40 minutes, 5 hours
Salvatore et al[109]	□	●	1 (0)	●	●	■	●	● 1–30 days ○ 1–140 days

(*Continued*)

TABLE 2. (*Continued*)

Study	Design*	Patients†	N (% Female)	INT‡	Outcome			Pre-post follow-up interval/s#
					OBJ§	SBJ‖	PSE/QOL¶	
Sanuki and Isshiki[110]	○	●	41 (85)	○	○	■	○	● ○ 12–53 months
Sanuki et al[111]	●	●	15 (100)	○	●	○	●	● ○ Mean 30.1 months
Sanuki et al[112]	●	●	10 (100)	○	●	○	○	● ○ 6 months
Sapienza et al[113]	●	●	31 (84)	●	●	■	○	● No more than 2 weeks ○ mean 33 days (range = 3–6 weeks)
Schonweiler et al[114]	●	●	8 (50)	●	●	●	○	● 1 week ○ 4 weeks +/- 3 days
Shaw et al[115]	□	○	3 (100)	○	○	■	○	● ○ 2 weeks, 3 months, 1 year
Silverman et al[116]	●	●	31 (84)	●/●+□	●	■	●	● ○ 3, 7, and 12 weeks, immediately prior to re-injection
Simonyan and Frucht[117]	□	●■	1 (100)	■	●	●	○	● ○ 90 minutes, 8 months
Srirompotong et al[118]	○	●	37 (89)	●	○	●	○	● ○ 14 days
Su et al[119]	●	●	14 (86)	○	●	■	○	● ○ 1–2 weeks and 1, 3, 6, 12, 18, 24 months
Su et al[120]	●	●	29 (79)	○	●	■	○	● 1–2 weeks ○ 1, 3, 12, 18, 24, 36, 48, and 60 months
Sulica et al[121]	○	●	16 (75)	○ +/- ●	○	●	○	● ○ UD
Tisch et al[122]	●	●○□	169 (62)	●	●	●■	○	● ○ UD
Truong et al[123]	●	●	13 (UD)	●	●	■	○	● ○ ~4 days
Tsuji et al[124]	●	●	7 (86)	○	○	○	●	● ○ Mean 23.7 months
Tsuji et al[125]	●	●	15 (73)	○	○	○	●	● ○ 4–96 months
Tsunoda et al[126]	□	●	1 (0)	○	●	○	○	● ○ 1 year
Wang and Lu[127]	●	●, ●■	9 (78)	●	●	■	○	● ○ 1 month
Whurr et al[128]	●	●	31 (65)	●	●	●	○	● ○ Mean 10 weeks (range = 2–30 weeks)
Whurr et al[129]	●	UD	46 (65)	●	●	○	●	● ○ 6 months
Wilson et al[130]	□	●	1 (100)	○	○	■	○	● ○ 12 hours, 3 months
Wingate et al[131]	●	●	13 (100)	●	○	○	●	● ○ 4 weeks
Witsell et al[132]	●	●	15 (73)	●	●	○	○	● ○ 2 weeks, 3 months
Wong et al[133]	●	●	17 (65)	●	●	○	○	● ○ 2 and 10 weeks
Woo et al[134]	●	●	18 (UD)	●	●	■	○	● ○ Immediately post, 4 weeks, immediately prior to re-injection
Woodson et al[135]	●	●	17 (UD)	●	●	○	○	● ○ 1 month
Young and Blitzer[136]	□	●	4 (75)	●	○	●	○	● ○ UD
Zwirner et al[137]	●	●	19 (79)	●	●	○	○	● 1 week ○ 1 week
Zwirner et al[138]	●	●	11 (91)	●	●	■	○	● 1 week ○ 1 week, 1 month
Zwirner et al[139]	●	●	19 (79)	●	●	■	○	● 1 week ○ 1 week
Zwirner et al[140]	●	●	24 (79)	●	●	●	○	● 1 week ○ 1 week, 1 month
Zwirner et al[141]	●	●	16 (81)	●	●	○	○	● 1 week ○ 7–10 days

* Design: ○ retrospective; ● Prospective; □ Case study/case series; UC, unclear whether retrospective or prospective.
† Patients: ○ AB SD; ● AD SD; □ Mixed; ●■AD SD + VT; ○■ AB SD + VT.
‡ Intervention (INT): ● Botox; ○ Surgery; ■ Drug therapy; □ Other.
§ Objective (OBJ) outcome measure: ● Yes; ○ No.
‖ Subjective (SBJ) outcome measure: ● Patient as rater; ■ Experienced rater; □ Novice rater; ○ No subjective voice measures reported.
¶ Psycho-social-emotional/quality-of-life (PSE/QOL) outcome measure: ● Yes; ○ N.
# Pre-post follow-up interval/s: ● Pre; ○ Post.
Abbreviations: N, number of participants with pre-post data reported; UD, undisclosed.

reliability and validity as it pertains to the SD population has been made where appropriate. However, it is important to note that merely having undergone some process of measurement validation does not guarantee quality.[17]

Within the ICF framework, the vast majority of outcome instruments related to body functions (n = 212) were measures of "impairment." "Impairment" is defined as an abnormality in physical function (eg, abnormal laryngeal function represented perceptually through SD-characteristic voice breaks). Within this component, most instruments were either objective measures of voice functioning comprising acoustics (n = 77), aerodynamic measures (n = 14), electroglottography (EGG) (n = 7), EMG (n = 7), and vocal fold imaging (n = 8) or subjective measures of vocal performance as reported by the patient (n = 18), or experienced or novice (n = 52) listeners. Although perceptual measures of voice quality have traditionally been reported as a measure of speech activity (see below), the majority of perceptual measures identified in this study rated the degree of impairment and have therefore been classified as "Body Function." A single study conducted by Dromey et al[54] used articulatory kinematics to report the duration of articulatory movement, lip and jaw displacement, the amplitude and velocity of upper- and lower-lip displacement, the spatiotemporal index, and counts of velocity peaks (n = 9). Brain imaging (functional magnetic resonance imaging and positron emission tomography) was used in three studies to compare preintervention and postintervention changes in regional cerebral blood flow[24] and areas of sensorimotor activation.[69,117] Also categorized within the Body Functions domain were measures of cognitive and/or psychological function (n = 18). These encompassed measures of psychological and somatic complaints including depression, anxiety, mood, and stress (see Table 3). These were seldom repeated across studies, with only the Self-rating of Depression Scale[158] and State Anxiety Inventory[161] being used in more than one study. Of the measures used, 80% (17/19) were psychometrically reliable and validated scales; however, only the Glottal Function Index[149] has been validated using an SD population. The Somatic Complaints Checklist[160] was developed specifically for the SD population, focusing on symptoms that are frequently reported by patients with SD as per the literature and clinical experience.

Within the Activity and Participation ICF domains, eight outcome instruments were identified. These were related to communication and participation in everyday life and attitudes toward communication (see Table 3). The ICF model defines "activity" as the execution of a task or action by an individual, with an "activity limitation" being a limitation in performance caused by the impairment (eg, inability to produce a voice with a clear quality so it can easily be heard). "Participation" is defined within the ICF model as involvement in life situations, where "participation restriction" refers to a loss of role function because of the impairment (eg, no longer able to perform a job as required). Seven activity and participation measures were patient-rated (see Table 3). However, only the Speech Disability Questionnaire[56] was specifically developed for use with the SD population. Four outcome instruments also captured quality of life, a construct that does not fall within the ICF: Voice Activity and Participation Profile,[163] Voice Handicap Index (VHI[164]), VHI-10,[165] and Voice-Related Quality of Life (VRQOL[166]). The VHI was the most commonly used (n = 17), with data being collected pretreatment and at a range of 1 day up to 11 years posttreatment. Forty-one percent (n = 7/17) of studies using the VHI repeated the measure at two posttreatment intervals. Eight studies used the VRQOL, with follow-up intervals ranging between 2 days and 12 weeks.

Although activity and participation is typically measured using self-rated scales, two studies used experienced raters to measure speech intelligibility[30] and functional status (ie, the impact of the disorder on an individuals' ability to communicate[138]). Dykstra et al[167] have argued that as the exact relationship between speech subsystem physiology and speech intelligibility has yet to be determined, speech intelligibility is more easily conceptualized from an activity level rather than body function.

The SF36,[159] a general health-related questionnaire that does not focus specifically on communication disorders, fell across the Body Function, Activity, and Participation domains (see Table 3).

Despite measures of the communication partners' perspective or burden/disability experienced by communication partners of people with SD being within the scope of this review, no outcome instruments that measure constructs that could be categorized as solely evaluating environmental factors were identified.

The following sections elaborate further on the frequency and/or characteristics of the extracted outcome instruments that fall under the "Body Functions" domain.

Acoustics

Fifty-four (43%) studies used some form of acoustic outcome instrument(s). Across these studies, 77 different outcome instruments were reported, with 61% (n = 47) having only a single occurrence. Acoustic parameters used by more than one study are outlined in Table 4.

Aerodynamics

Aerodynamic analysis incorporates the measurement of airflow and air pressure, and their relationship during phonation (see Table 5). Fourteen different aerodynamic parameters were investigated across 34 studies. The simplest aerodynamic parameter of voice, maximum phonation time (in seconds), was reported in 22 studies. Mean airflow rate and laryngeal resistance were also commonly measured (14 and 4 studies, respectively). Vocal efficiency (ie, the ratio of acoustical power to aerodynamic power) was reported in one study.[112] Details regarding the procedure of data capture and/or assessment stimulus were not explicitly reported in all studies (see Table 5).

TABLE 3.
Cognitive, Psychosocial-Emotional, or Quality-of-Life Measures

Outcome Instrument	WHO ICF	Admin	Format/Scoring	Reference
Beck Depression Inventory (BDI[143])	BF	P	A 21-item questionnaire that describe the somatic, behavioral, and cognitive symptoms of depression. Patients respond based on how they have felt during the last week, selecting the statement that best matches his/her feelings. Each statement has a set of at least four possible responses options, ranging in intensity. A value of 0–3 is assigned for each response. Higher total scores indicate more severe depressive symptoms.	Whurr et al[129]
Buffalo III Speech Anxiety Profile[144]	BF	C	A 5-factor scale (1 = normal up to 5 = very severe) developed for the assessment of amount and degree of speech anxiety in children.	Epstein et al[55]
Columbia Suicide Severity Rating Scale (C-SSRS[145])	BF	C	A six-yes/no-question measure used to rate an individuals' degree of suicidal ideation ranging from "desire to be dead" to "active suicidal ideation with specific plan and intent." Answering "yes" to any of the six questions may indicate need for mental health referral.	Rumbach et al[108]
Crown Crist Experiential Index (CCEI[146])	BF	P	A 48-item questionnaire designed to measure neurotic symptomatology. There are six subscales (free-floating, anxiety, phobic, obsessional, somatic, depressive, and hysteria), each containing eight items. On each subscale, higher scores indicate more neurotic symptoms. Subscores can be combined to form an overall score of neurotic pathology.	Whurr et al[129]
Epworth Sleepiness Scale (ESS[147])	BF	P	An eight-item questionnaire designed to evaluate daytime sleepiness. Respondents are asked to rate, on a four-point scale (0 = would never doze; 3 = high chance of dozing), their usual chances of dozing off or falling asleep while engaged in eight common activities (eg, watching television, sitting, and talking to someone). Overall scores of 0–10 indicate normal daytime sleepiness.	Rumbach et al[108]
Erickson Scale of Communication Attitudes (ESCA[148])	A + P	P	A 24-item true/false questionnaire designed to evaluate subjects' attitudes to communication. The ESCA was originally developed and validated for use with adults who stutter. Modifications to wording of statements was made to make the scale more appropriate for a SD population. ESCA scores are the sum of all negatively valenced responses.	Cannito et al[43]
Glottal Function Index (GFI[149]) ◆	BF	P	Four-symptom index aimed at assessing symptoms of glottal dysfunction (0 = no problem, 5 = severe problem). Subjects are asked to rate the level of effort when speaking, throat discomfort/pain after talking, vocal fatigue, and voice cracks/sounds different within the last month. A GFI higher than 4 is considered abnormal.	Koufman et al[81]
GHQ/QL-12[150]	BF	P	A 12-item screening questionnaire for identifying non-psychotic and minor psychiatric disorders. Higher scores indicated better life quality.	Liu et al[86]
Hamilton Anxiety Rating Scale (HARS[151])	BF	C	A 14-item scale designed to assess the severity of symptoms of anxiety. Each item is scored on a scale of 0 (not present) to 4 (severe). Higher scores indicate more anxiety.	Liu et al[86]
Hamilton Depression Rating Scale (HDRS[152])	BF	C	A 17-item scale designed to assess severity of, and change in, symptoms of depression. Each item is scored by the clinician selecting the "cue" (rated from 0–2 or 0–4) which best characterizes the patient. Higher scores indicate more depression. A score of 0–7 is generally accepted to be within normal limits.	Liu et al[86]

(*Continued*)

TABLE 3. (*Continued*)

Outcome Instrument	WHO ICF	Admin	Format/Scoring	Reference
Hopkins Symptom Checklist—Dutch Version (HSCL[153])	BF	P	A 57-item symptom rating scale designed to assess and monitor psychological and somatic complaints. Subjects respond using a 4-point scale of distress: "not at all" (score of 1) to "extreme" (score of 4). The explicit temporal referent of "How have you felt during the past seven days including today?" is used. Higher scores indicate more distress.	Langeveld et al[83]
Montreal Cognitive Assessment (MoCA[154])	BF		A 30-item test screening instrument designed to detect mild cognitive impairment. It assesses eight cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. The total possible score is 30; a score of 26 or above is considered normal.	Rumbach et al[108]
Mini-Mental State Examination (MMSE[155])	BF		A 30-item questionnaire used to measure cognitive impairment. Functions examined include orientation to time and place, registration and recall, attention and calculation, language use and comprehension, and basic motor skills. A score greater than or equal to 24 out of 30 possible points indicates normal cognition.	Rumbach et al[108]
Mood Adjective Checklist (MACL[156])	BF	P	A survey of 24 mood-related adjectives related to tension/anxiety, anger/hostility, depression, fatigue/inertia, and vigor/activity. Patients indicate their moods in the last 24 hours using a 4-point scale to rate each adjective: "not at all" (score of 0), "a little" (score of 1), "quite a bit" (score of 2), "extremely" (score of 3). Higher scores indicate a more negative mood.	Whurr et al[129]
Perceived Stress Scale (PSS[157])	BF	P	A 10-item survey designed to measure a subjects' perception of stress. Subjects' indicate how often they felt or thought a certain way during the last month using a five-point scale: "never" (score of 0), "almost never" (score of 1),"sometimes" (score of 2), "fairly often" (score of 3), "very often" (score of 4).	Paniello et al[101]
Self-rating of Depression Scale (SDS[158])	BF	P	A 20-item survey designed to assess a patient's level of depression. Each item is rated on a four-point Likert scale: "little of the time" (score of 1), "some of the time" (score of 2), "a good part of the time" (score of 3), "most or all of the time" (score of 4). Scores over 50 indicate the presence of depression.	Liu et al[86]; Murry et al[97]
Speech Disability Questionnaire (SDQ[56])	A + P	P	A 28-item self-administered questionnaire that aims at assessing activity limitation and participation resulting from a speech disorder. Areas of relevance to SD include occupation, family, and social interaction.	Epstein et al[56]
Short Form 36-Item Health Survey (SF36[159])	BF A + P	P	A 36-item questionnaire designed to evaluate health status. Consists of eight scale scores: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, and mental health. The lower the score, the greater the disability.	Courey et al[48]
Somatic Complaints Checklist◆[160]	BF		A 26-item questionnaire that consists of symptoms frequently reported by people with SD, as determined from the literature and clinical experience. Each item is rated on a five-point Likert scale anchored by "never" (score of 0) and "always" (score of 4). Possible scores range from 0 to 108. Symptoms that have worsened in association with the voice disorder are marked with an asterisk.	Murry et al[97]

(*Continued*)

TABLE 3. (*Continued*)

Outcome Instrument	WHO ICF	Admin	Format/Scoring	Reference
State Anxiety Inventory (STAI[161])	BF	P	Forty items used to measure state and trait anxiety. All items are rated on a four-point Likert scale anchored by "Almost Never/Not at all" (score of 1) to "Almost Always/Very much so" (score of 4). Higher scores indicate greater anxiety.	Epstein et al[55]; Murry et al[97]
SCL-90: Symptom Distress Checklist[162]	BF	P	A 90-item questionnaire designed to evaluate a range of psychological problems and symptoms of psychopathology. Patients indicate how much they have been bothered by symptoms (eg, headaches) in the last week hours using a five-point scale: "not at all" (score of 0), "a little bit" (score of 1), "moderately" (score of 2), "quite a bit" (score of 3), "extremely" (score of 4). Higher scores indicate more distress.	Liu et al[86]
Voice Activity and Participation Profile (VAPP[163])	A + P	P	A 28-item assessment tool that evaluates the perception of voice problem, activity limitation, and participation restriction using the WHO ICIDH-2 framework. Overall severity of the voice problem and its effect on job, daily communication, social communication, and emotions are explored. Each statement is rated using a visual analogue scale anchored by "normal/never" and "severe/always."	Salvatore et al[109]
Voice Handicap Index (VHI[164])	A + P		Thirty statements, grouped into functional, emotional, and physical subscales. Each statement is individually scored on a five-point Likert scale anchored by "never" (score of 0) and "always" (score of 4).	Anari et al[26]; Benninger et al[31]; Courey et al[48]; Dejonckere et al[53]; Esposito et al[57]; Geneid et al[66]; Ghandi et al[65]; Hussain & Shakeel[72]; Kim et al[77]; Kim et al[78]; Morzaria & Damrose[96]; Novakovic et al[12]; Remacle et al[103]; Rojas et al[105]; Tsuji et al[124]; Tsuji et al[125]; Wingate et al[131]
Voice Handicap Index-10 (VHI-10[165])	A + P	P	10 statements grouped into functional, emotional, and physical subscales. Each item is individually scored on a five-point Likert scale anchored by "never" (score of 0) and "always" (score of 4).	Hartmann et al[68,*]; Morzaria & Damrose[96]; Nomoto et al[100]; Sanuki et al[111]
Voice-Related Quality of Life (VRQOL[166])	A + P	P	A 10-item survey investigating the impact of the voice disorder on quality of life. Patients respond based on their voice over the past 2 weeks. Subscales are Social-Emotional and Physical Functioning. Administration time is approximately 5 minutes. Each item is individually scored on a five-point Likert scale: (1) none, not a problem, (2) a small amount, (3) a moderate amount/problem, (4) a lot, (5) problem is "as bad as it can be."	Hogikyan et al[71]; Klein et al[79]; Morzaria & Damrose[95]; Morzaria & Damrose[96]; Paniello et al[101,†]; Rubin et al[107]; Paniello et al[102]; Silverman et al[116];

* VHI-12.
† Included VRQOL singing and swallowing supplements.
◆ Developed and/or validated using an SD population.
Abbreviations: A + P, Activity and Participation; BF, Body Function; C, clinician; P, Patient; GHQ/QL-12, General Health Questionnaire/Quality of Life-12.

TABLE 4.
Acoustic Measures

Parameter		N	Reference
Fundamental Frequency	Mean	21	Adams et al[21]; Adams et al[22]; Crevier-Buchman et al[49]; Ford et al[61]; Ford et al[62]; Fritzell et a[63]; Haslinger et al[69]; Isshiki et al[73]; Kendall & Leondard[76]; Kim et al[77]; Langeveld et al[84]; Mehta et al[92]; Rhew et al[104]; Rontal et al[106]; Su et al[119]; Su et al[120]; Truong et al[123]; Wang & Lu[127]; Whurr et al[129]; Zwirner et al[137]; Zwirner et al[139]
	Range	2	Kendall & Leonard[76]; Truong et al[123]
	Standard deviation (SDF0)	16	Adams et al[22]; Crevier-Buchman et al[49]; Kendall & Leonard[76]; Langeveld et al[84]; Mehta et al[92]; Murry & Woodson[98]; Sanuki et al[111]; Sanuki et al,[112] Schonweiler et al[114]; Whurr et al[128]; Whurr et al[129]; Zwirner et al[137]; Zwirner et al[138]; Zwirner et al[139]; Zwirner et al[140]; Zwirner et al[141]
	Tremor intensity	2	Kim et al[77]; Wang & Lu[127]
	Variability	3	Abdoerrachman[19]; Haslinger et al[69]; Rontal et al[106]
	Percentage of frequency shifts	2	Cannito et al[42]; Sapienza et al[113]
Pitch	Range	3	Kaszas et al[75]; Schonweiler et al[114]; Tisch et al[122]
	Number of pitch breaks	4	Ali et al[24]; Ludlow et al[87]; Ludlow et al[88]; Rhew et al[104]
Intensity	Range	4	Ford et al[61]; Kaszas et al[75]; Langeveld et al[84]; Schonweiler et al[114]
Phonation	Number of phonation/voice breaks	9	Ali et al[24]; Allegretto et al[25]; Hartmann et al[68]; Ludlow et al[87]; Ludlow et al[88]; Rhew et al[104]; Rontal et al[106]; Sapienza et al[113]; Schonweiler et al[114]
	Percentage of phonation/voice breaks	4	Cannito et al[42]; Langeveld et al[84]; Sapienza et al[113]; Silverman et al[116]
	Degree of voice breaks (total duration of break between the voiced parts of the signal divided by the total signal duration)	3	Sanuki et al[111]; Sanuki et al[112]; Schonweiler et al[114]
	Voice break factor	6	Adams et al[21]; Adams et al[22]; Zwirner et al[137]; Zwirner et al[138]; Zwirner et al[139]; Zwirner et al[140]
Harmonicity	Noise-to-harmonic ratio	5	Crevier-Buchman et al[49]; Schonweiler et al[114]; Su et al[119]; Su et al[120]; Wang & Lu[127]
	Harmonic-to-noise ratio	5	Esposito et al[57]; Kim et al[77]; Kim et al[78]; Sanuki et al[111]; Sanuki et al[112]
Perturbation	Jitter	25	Adams et al[21]; Adams et al[22]; Boseley et al[38]; Crevier-Buchman et al[49]; Dejonckere et al[53]; Dromey et al[54]; Ford et al[61]; Ford et al[62]; Green et al[67]; Hartmann et al[68]; Kendall & Leonard[76]; Kim et al[78]; Mehta et al[92]; Meyers & Anderson[93]; Murry & Woodson[98]; Rontal et al[106]; Sanuki et al[111]; Sanuki et al[112]; Schonweiler et al[114]; Su et al[119]; Su et al[120]; Zwirner et al[137]; Zwirner et al[138]; Zwirner et al[139]; Zwirner et al[140]
	Shimmer	22	Adams et al[21]; Adams et al[22]; Boseley et al[38]; Crevier-Buchman et al[49]; Dromey et al[54]; Ford et al[61]; Ford et al[62]; Hartmann et al[68]; Kendall & Leonard[76]; Kim et al[78]; Mehta et al[92]; Meyers & Anderson[93]; Murry & Woodson[98]; Sanuki et al[111]; Sanuki et al[112]; Schonweiler et al[114]; Su et al[119]; Su et al[120]; Zwirner et al[137]; Zwirner et al[138]; Zwirner et al[139]; Zwirner et al[140]
	Amplitude of perturbation quotient	2	Abdoerrachman[19]; Wang & Lu[127]
Aperiodicity	Mean % aperiodicity	2	Ali et al[24]; Rhew et al[104]
	Duration of aperiodic segments	3	Ludlow et al[87]; Ludlow et al[88]; Sapienza et al[113]
	Percentage of aperiodic segments	3	Cannito et al[42]; Sapienza et al[113]; Silverman et al[116]
Timing	Total speaking time (accumulated duration of voices sounds and silence)	11	Crevier-Buchman et al[49]; Fritzell et al[63]; Fritzell et al[64]; Hartmann et al[68]; Langeveld et al[84]; Ludlow et al[87]; Ludlow et al[89]; Rhew et al[104]; Rontal et al[106]; Salvatore et al[109]; Whurr et al[129]
	Total pause time	2	Fritzell et al[64]; Salvatore et al[109]
	Speech rate (words/minute)	3	Crevier-Buchman et al[49]; Murry & Woodson[98]; Salvatore et al[109]
	Duration of periodic phonation	2	Ludlow et al[89]; Silverman et al[116]
	Accumulated voicing time	2	Fritzell et al[63]; Fritzell et al[64]
	Voiced segment duration (time from the onset of voicing to voicing offset within the words produced in reading, measured in milliseconds)	2	Sapienza et al[113]; Silverman et al[116]
	Total articulation time	2	Langeveld et al[84]; Salvatore et al[109]
Other	SNR	10	Adams et al[22]; Dromey et al[54]; Ford et al[61]; Ford et al[62]; Mehta et al[92]; Murry & Woodson[98]; Zwirner et al[137]; Zwirner et al[138]; Zwirner et al[139]; Zwirner et al[140]
	Visual inspection of spectographic profile	4	Dedo & Behlau[51]; Rojas et al[105]; Truong et al[123]; Tsunoda et al[126]

Abbreviation: SNR, Signal-to-noise ratio.

TABLE 5.
Aerodynamic Measures

Study	Stimulus	Parameters* Reported			
		MAR	MPT	LR	Other
Adams et al[21]	Sustained phonation on /ah/	○	●	○	
Adams et al[22]	Sustained phonation on /ah/	○	●	○	
Adams et al[20]	Syllable repetition of /pi/ seven times in succession while maintaining a loudness level of approximately 70 dB. Each subject produced three sets of seven repeated syllables.	●	○	●	Intraoral pressure
Boseley et al[38]	Not reported	○	●	○	
Cantarella et al[45]	Sustained phonation on /ah/ for at least 3 seconds	●	○	○	Coefficient of variation of airflow
Crevier-Buchman et al[49]	Sustained phonation on /ah/	○	●	○	
Dromey et al[54]	Syllable repetition of /pa/ five times on one continuous breath while using a constant vocal effort, at a rate of approximately 90 syllables per minute. Each subject repeated the task three times.	●	○	○	Intraoral pressure
Esposito et al[57]	Sustained phonation on /ah/	○	●	○	
Finnegan et al[58]	Syllable repetition of /pi/ in a continuous manner at 1.5 syllables per second.	●	○	○	Coefficient of variation of airflow
Fisher et al[59]	Syllable repetition of /pa/ five times at a rate of 1.5 syllables per second. The subject performed at least three task repetitions for each normal and loud conditions.	○	○	○	Flow open quotient Peak-to-peak flow value Maximum negative peak value Flow peak quotient Peak baseline (DC) flow
Ford et al[61]	Sustained phonation on /ah/	○	●†	○	
Ford et al[62]	Sustained phonation on a vowel	○	●	○	
Green et al[67]	Syllable repetition of /pi/ seven times. Each subjected repeated the task three times. For each task repetition, subjects were instructed to take a break of twice the normal depth and produce the seven productions on a single, continuous expiration at normal loudness, pitch, and quality, with equal stress on each syllable at an utterance rate of 1.5 syllables/sec as paced externally.	○	○	●	
Kaszas et al[75]	Not reported	○	●	○	
Kim et al[78]	Not reported	○	●	○	
Kim et al[79]	Not reported	●	○	●	
Langeveld et al[84]	Sustained phonation on /ah/	○	●	○	
Mehta et al[92]	Sustained phonation on /ah/, performed three times. Airflow rates were calculated using the average of first 3 seconds of each of the three samples.	○	●	○	Translaryngeal airflow
Miller et al[94]	Quiet respiration, phonation, Valsalva's maneuver	○	○	○	Intrathoracic pressure
Murry & Woodson[98]	Sustained phonation on /ah/	●	○	○	
Sanuki et al[112]	Sustained phonation on /ah/	●	○	○	Voice efficiency
Schonweiler et al[114]	Not reported	○	●	○	
Su et al[119]	Sustained phonation on /ah/	●	●	○	
Su et al[120]	Sustained phonation on a vowel	●	●	○	
Tisch et al[122]	Sustained phonation on /ah/	●	●	○	
Truong et al[123]	Sustained phonation on /ah/	○	●	○	
Tsunoda et al[126]	Not reported	○	●	○	
Wang & Lu[127]	Sustained phonation on /ah/	●	○	○	s/z ratio
Witsell et al[132]	Syllable repetition on /pi/ five to eight times in an evenly spaced midvolume manner. Three to five sets of /pi/ phonation were completed before calculating mean laryngeal resistance.	○	○	●	
Woo et al[134]	Sustained phonation on /i/	●	●	○	
Zwirner et al[137]	Sustained phonation on /ah/	○	●	○	
Zwirner et al[138]	Sustained phonation on /ah/	●	●	○	
Zwirner et al[139]	Sustained phonation on /ah/	○	●	○	
Zwirner et al[140]	Sustained phonation on /ah/	●	●	○	

* Parameter = ● Yes; ○ No.
† Maximum phonation time before voice break.
Abbreviations: MAR, mean airflow rate; MPT, maximum phonation time; LR, laryngeal resistance; DC, unmodulated pulmonary airflow.

Adjuvant techniques: EGG and EMG

EGG was used in three studies[59,60,93] to monitor vocal fold contact, rate of vibration, and perturbation of regularity during voice production in patients with AD SD. Meyers and Anderson[93] investigated the efficacy of a stuttering therapy program using a single case study design. Prelaryngographic and postlaryngographic measures for prolonged /i/, reading, and spontaneous speech included variability per phonation stretch, shape of the Lx waveform, shimmer, fundamental frequency, jitter, abnormal fundamental frequency drops, and vocal fry. Fisher et al[59] and Fisher et al[60] used EGG measures to examine change over time before and 3 weeks after botulinum toxin injection. Both studies used the same stimulus and analysis procedure: five syllable repetition of /pa/ with the vowel portion of the fifth syllable elongated > 2 seconds in normal and loud conditions with analysis initiated at least 200 ms after voicing onset. This allowed the extraction of data for the following parameters: (1) duty cycle measure of waveform width at the 50% amplitude level (EGGW50); (2) the nondimensional opening slope measurement between the 90% and 50% amplitude levels on the downward or glottal opening side (SP9050); (3) the nondimensional closing slope measurement between 10% and 90% of the waveform amplitude level on the upward or glottal closing side (SC1090); and (4) a slope quotient (SLQ), which was the ratio of SC1090 to SO9050. However, in the later study[60] they noted that SC1090 and SLQ measures were unstable in some patients and therefore were not reported.

EMG, an electrophysiological investigation of neuromuscular function, was used in seven studies[34,63,64,70,87,91,92] in varying ways. Henschen and Burton,[70] using progressive relaxation as the treatment modality, used EMG both as a biofeedback tool and as a way of measuring treatment efficacy. External electrode placement was used to examine laryngeal and forehead tension over time, with the findings being largely descriptive, reporting the lowest microvolt reading registered during each of the baseline and training sessions. Fritzell et al[63] and Fritzell et al[64] descriptively compared EMG activity of the cricothyroid and vocalis muscles before and after the excision of the recurrent laryngeal nerve in patients with AD SD. Descriptive reporting of EMG findings was similarly used by Maronian et al,[91] who evaluated the effect of botulinum toxin injection on the presence and absence of vocal breaks and tremor and latency between the onset of muscle activity and voicing. The muscles examined varied across injections and between patients, with recordings from the thyroarytenoid (TA), lateral cricoarytenoid, posterior cricoarytenoid, interarytenoid, and cricothyroid (CT) possible. Individual datum was analyzed to determine which muscle was the most active and which muscle was predominately active in breaks and tremor. Mehta et al[92] was the only study to employ a three-point severity scale of inappropriate muscle activity (IMA) during phonation (ie, 1 = little to no IMA; 2 = low-amplitude IMA; and 3 = high-amplitude IMA) with EMG signals being graded by the treating otolaryngologist and speech-language pathologist before and after botulinum toxin injection. However, like in Maronian et al,[91] the muscles examined varied across injections and between patients. Two studies, Bielamowicz and Ludlow[34] and Ludlow et al,[87] employed seemingly more rigorous EMG methodology, providing procedural information for electrode insertion and placement verification for the TA and CT muscles as well as detailed information regarding signal analysis. Ludlow et al[87] examined minimum, maximum, and mean levels of muscle activity in microvolts during quiet respiration and speech tasks. Similarly, mean resting activity (ie, quiet respiration), maximum muscle activation level, and mean percent of maximum activity during phonation were calculated in Bielamowicz and Ludlow.[34] Additionally, the number of muscle bursts, defined as sustained activity two times that of surrounding activity and between 50 and 100 ms in duration, were measured. Repeated multifactorial analysis of variance comparisons across subjects before and after botulinum toxin injection were performed.

Vocal fold imaging

As laryngoscopy +/− stroboscopy can be used to assess the quality of vocal fold vibration, it may be useful to evaluate the effectiveness of treatment. Videolaryngoscopic and videostroboscopic parameters should have good interrater and intrarater reliability, and thus, it is classically recommended that grading scales, quantitative measurements, and multiple raters be utilized. A total of 13 studies specifically reported laryngoscopic findings before and after intervention, with five reporting results descriptively only.[57,73,93,104,126] Parameters descriptively reported included the presence or absence of AD or AB spasms, tremor, anterior-posterior compression, and false vocal fold approximation. Wong et al[133] objectively compared laryngeal activity before and after botulinum toxin using software to select specific points from a still image and translating these into Cartesian coordinates, using the width of the right aryepiglottic fold in each image as a calibration standard. The calculated parameters included anterior-posterior glottic diameter, right and left vocal cord widths, the distance between the false vocal folds, and the glottal area. The remaining seven studies used a variety of ordinal rating scales (see Table 6). There was a small degree of uniformity in scales across studies, with Schonweiler et al,[114] Su et al,[120] and Zwirner et al[138] all using scales consistent with or adapted from those outlined in Woodson et al[135] for their analysis. However, the wording and level of detail provided for rating descriptors were inconsistent across studies (see Table 6). Although the study published by Su et al[119] rated the same parameters as presented in Su et al[120] and reported the use of a four-point ordinal rating scale, there was no reference made to the origin of the rating scale and therefore, for the purposes of this study, must be considered a separate rating method. Kim et al[77] used a purpose-built scale (see Table 6). Schonweiler et al[114] and Woodson et al[135] were the only two studies that reported the use of multiple raters to obtain the final data reported (four and two experienced raters, respectively). The degree of interrater reliability was not reported.

TABLE 6.
Scales Used to Rate Parameters Identified on Laryngoscopic Examination

Scale	Parameters Rated	Reference
N = within normal limits or D = decrease (adduction and mucosal wave); + = greater than preop status or 0 = nearly same (gap between intervocal process during phonation)	• Range of adduction • Production of mucosal wave during phonation • Gap between intervocal processes	Kim et al[77]
Ventricular compression (adapted from Woo et al[134]; Woodson et al[135]; Zwirner et al[138]): 0 = absent; 1 = mild/on initiation of phonation/one third of the vocal folds covered on entire phonation; 2 = moderate/two thirds of the vocal folds hidden on entire phonation; 3 = severe/vocal folds nearly hidden on entire phonation. Anterior-posterior compression (adapted from Woodson et al[135]): 0 = absent; 1 = on initiation of phonation/mild on entire phonation; 2 = moderate on entire phonation; 3 = severe on entire phonation Incomplete closure of the vocal folds (adapted from Woo et al[134]; Zwirner et al[138]): 0 = absent/complete closure; 1 = mild/just notable to less than or equal to 1 mm; 2 = moderate/approximately 1–2 mm; 3 = severe/approximately greater than 2 mm	• Ventricular compression • A-P compression • Incomplete closure of the vocal folds	Schonweiler et al[114]
Four-point scale, adapted from Woodson et al[135] (0 = normal appearance; 3 = most severe dysfunction)	• Mucosa wave patterns • Wave amplitude • Periodicity • Glottal closure • Supraglottic compression • Presence of tremors during phonation	Su et al[120]
Four-point scale (0 = normal appearance; 3 = most severe dysfunction)	• Mucosa wave patterns • Wave amplitude • Periodicity • Glottal closure • Supraglottic compression • Presence of tremors during phonation	Su et al[119]
Four-point scale of compression (0 = none, 1 = slight, 2 = moderate, 3 = full)	• A-P compression • Ventricular hyperfunction	Woo et al[134]
Ventricular compression: 0 = absent; 1 = one third of the true vocal folds are covered on phonation; 2 = two thirds of the true vocal folds on phonation; 3 = true vocal folds are totally covered on phonation. Anterior-posterior compression: 0 = absent (vocal folds are not shorter than during quiet respiration); 1 = mild on phonation; 2 = moderate on phonation; 3 = severe on phonation Note: pictorial descriptors of each normal-mild-moderate-severe levels of A-P compression are provided within the original article.	• Excessive phonatory activation of intrinsic laryngeal muscles as indicated by excessive arytenoid adduction, abduction, or vocal fold rigidity. • Extrinsic muscle hyperfunction as indicated by degree of false vocal fold compression during phonation • A-P compression • Tremor during respiration/phonation or spasmodic movements during respiration was noted	Woodson et al[135]
Four-point scale as per Woodson et al[135] (0 = normal function, 3 = very abnormal)	• Intrinsic muscle hyperfunction • Extrinsic hyperfunction • Tremor during respiration/phonation or spasmodic movements during respiration was noted	Zwirner et al[138]

Abbreviation: A-P, Anterior-posterior.

TABLE 7.
Patient-Rated Scales

	Scale	Parameters Rated	Reference
Ordinal/Interval Scales	1 = normal, 2 = mildly impaired, 3 = mildly to moderately impaired, 4 = moderately impaired, 5 = moderately to severely impaired, 6 = severely impaired, 7 = very severely impaired (presented to patients as VAS using end points of "normal" and "very severely impaired"; interpreted as ordinal scale)	Sound of voice, physical effort needed to produce voice	Aronson et al[29]
	1 = most severe, 7 = normal	Vocal symptoms, degree of vocal effort	Chan et al[46]
	1 = excellent, 5 = terrible	Overall voice quality	Ford et al[61]
	Poor, fair, good, very good, excellent	Overall voice quality	Hogikyan et al[71]; Rubin et al[107]
	Equal interval scale from 0 to 10, with responses closer to 0 representing symptoms as less severe, and closer to 10 representing symptoms as more severe	Vocal spasms, hoarseness, breathiness, volume, swallowing	Liu et al[85]
	0 = absent/normal, 1 = mild, 2 = moderate, 3 = severe	Strangled voice quality, breathiness	Schonweiler et al[114]
	Mild, moderate, severe, or very severe	Overall severity	Tisch et al[122]
VASs	"Normal"[1] to "very severely impaired"[7]	Sound of voice, effort to speak	Adler et al[23]
	"Worst ever" to "best ever"	How the voice sounds, how the voice feels, degree of effort to produce voice	Fisher et al[59]
	"Bad" to "good" or "no" to "severe"	Intelligibility of speech, fluency of speech, breathy dysphonia, swallowing problems	Langeveld et al[82]
	"Severe/poor" to "normal/good"	Intelligibility of speech (conversational speech, during a party, in a public gathering), fatigue (tiring and shortness of breath), loudness, mode of phonation (fluency and strain) and side effects (eg, hoarseness, breathiness, dysphagia)	Langeveld et al[84]
	"Bad/extremely pathological" to "good/normal"	Intelligibility, effort, fluency of speech	Langeveld et al[83]
	"No effort"[1] to "constant struggle"[10]	Overall effort during speaking	Rumbach et al[108]
	"Normal"[1] to "most difficult"[10]	Effort during speaking, crying, and shouting	Simonyan and Frucht[117]
	"Worst possible voice" to "best possible voice"	Overall voice quality	Young and Blitzer[136]

Self-evaluation (ie, patient rated) measures of vocal performance

Thirty-four studies used patient self-evaluation to determine treatment efficacy and patient satisfaction with outcomes (see Table 2). Seventeen different outcome instruments were extracted. Important to note is that a number of studies described treatment effect as reported by the patient but either failed altogether to utilize a reproducible, standardized measure (eg,[28,63,72]) or did not provide detail regarding the measure used (eg,[62]); these were not included in the count of extracted instruments. Fifteen different ordinal, interval, or visual analogue scales (VASs) were used by patients to rate their voice quality and effort speaking across 16 different studies (see Table 7). Hogikyan et al[71] and Rubin et al[2] were the only two studies to use identical scales to judge the same parameter, "overall voice quality."

Tracking of patient response to treatment was also performed in 10 studies using "Percent of Normal Function" (PNF), a validated, quantitative, global VAS where 100% is the normal voice and 0% is the inability to phonate, with ratings being performed before and after treatment (eg,[10,35–37,118,121]) or from the day of treatment.[12,39,40,128] PNF was also used in two additional studies[124,125] to rate improvement posttreatment only. The explicit use of daily and/or weekly diaries starting

TABLE 8.
Clinician-Rated Ordinal/Interval Scales

	Scale	Parameters Evaluated	Stimulus	Reference	Blinded	Reliability	
						Inter	Intra
Three-point	1 = absent to mild; 2 = mild to moderate; 3 = moderate to severe	Overall severity of dysphonia, strained voice quality, voice breaks, dysfluency	UC	Berke et al[32]	UC	○	○
	1 = mild, 2 = moderate, 3 = severe	Breathiness spasticity	UC	Dedo and Behlau[51]	UC	○	○
		Overall voice	UC	Lundy et al[90]	UC	○	○
			Sustained phonation, phonation with pitch variations, conversation, reading, whispering, singing, laughing	Wang and Lu[127]	UC	○	○
	0 = normal, 1 = moderate, 2 = severe	Strangulation, interruption, tremor	Sustained /ah/	Sanuki and Isshiki[110]	UC	■	○
Four-point	0 = within normal limits; 1 = mild and occasional deviation from normal that would be intermittently noticeable to others; 2 = moderate deviation from normal that would detract from listener skills and disrupt speech at least once per sentence; 3 = severe deviation impairing speech intelligibility for communication	Overpressure, tremor, voice quality/roughness	We mow out lawn all year. A dog dug a new bone. The puppy bit the tape. Did he go to the right or to the left? When he comes home we'll feed him. Extended vowel.	Bielamowicz and Ludlow[34]	●	○	○
	0 = within normal limits; 1 = mild with occasional deviation from normal only intermittently noticeable to others; 2 = moderate deviation from normal that draws attention to itself; 3 = severe deviation from normal that would significantly impair speech intelligibility for communication	Breathiness, harshness, tremor	We mow out lawn all year. A dog dug a new bone. The puppy bit the tape. Did he go to the right or to the left? When he comes home we'll feed him. Extended vowel on /i/	Bielamowicz et al[33]	●	■	○
	Severely abnormal, moderately abnormal, mildly abnormal, normal (rated using a "sort and rate" computer program)	Breathiness, voice breaks	Sustained /ah/ Response to: "Describe your voice problem and how it affects you."	Chhetri et al[47]	●	●	●
	GRBAS: 0 = normal, 3 = worst	Grade, roughness, breathiness, asthenia, strain	UC	Gandhi et al[65]	UC	○	○
		Grade, roughness, breathiness, asthenia, strain	The North Wind and the Sun (Japanese)	Nakamura et al[99]	UC	○	○
		Grade, roughness, breathiness	The North Wind and the Sun (German)	Hartmann et al[68]	●	■	○
		Breathiness	"A rabbit suddenly appeared from the busy nearby" (Japanese); counting 1–10 (Japanese); sustained /ee/	Nomoto et al[100]	●	●	●
	0 = normal, 1 = mild, 2 = moderate, 3 = severe	Strain	UC	Kim et al[77]	UC	○	○
		Strangulation, interruption, tremor	"A rabbit suddenly appeared from the busy nearby" (Japanese); counting 1–10 (Japanese); sustained /ee/	Nomoto et al[100]	●	●	●

(*Continued*)

TABLE 8. (*Continued*)

	Scale	Parameters Evaluated	Stimulus	Reference	Blinded	Reliability	
						Inter	Intra
	0 = not impaired in normal lifestyle, 1 = mild or intermittent symptoms that did not significantly impair the patient's ability to communicate, 2 = noticeable disruption of speech with moderate impairment, 3 = severe disruption of speech that resulted in career or employment changes or decreased social interaction	Functional status (ie, impact of disorder on ability to communicate)	UC	Zwirner et al[138]	○	○	○
Five-point	0 = normal; 1 = mild; 2 = moderate; 3 = severe; 4 = profound	Overall severity of impairment	Oral reading (The Rainbow Passage)	Bender et al[30]	UC	■	○
				Cannito et al[41]	UC	■	○
	1 = mild (occasional overpressure with infrequent voice arrests); 2 and 3 = moderate severe (more obvious overpressure and more frequent voice arrests); 4 = severe (constant, marked overpressure and frequent voice arrests); 5 = most severe (nonsegmental syllabification of voice segments within each utterance).	Overall severity of impairment (spasticity)	UC	Dedo and Izdebski[52]	UC	○	○
	Buffalo Voice Profile III (Wilson, 1987): 1 = normal, 5 = very severe deviation	Muscle hypertense Laryngeal tone breathy Overall voice	UC	Epstein et al[56]	UC	■	○
	0 = no impairment; 4 = profound impairment	Overall voice	Spontaneous conversation, The Rainbow Passage, production of voiced phrases, laryngeal diadochokinetics, sustained vowels, /pa/ syllable string	Fisher et al[60]	UC	○	○
	0 = no impairment, 1 = mild dysphonia, 2 = moderate dysphonia, 3 = severe dysphonia, 4 = very severe dysphonia	Overall voice	The Rainbow Passage	Sapienza et al[113]	●	●	○
	1 = normal voice; 5 = voice quality that is extremely disordered	Overall voice	Sustained /ah/ and "We were away a year ago"	Silverman et al[116]	●	■	○
	0 = normal, 1 = mild dysfunction, 2 = moderate dysfunction, 3 = severe dysfunction, 4 = profound dysfunction	Overall grade, roughness, breathiness, interruption or break, strain, tremor	UC	Su et al[119]	UC	○	○
				Su et al[120]	UC	○	○

(*Continued*)

TABLE 8. (*Continued*)

	Scale	Parameters Evaluated	Stimulus	Reference	Blinded	Reliability	
						Inter	Intra
Six-point	0 = functionally aphonic, 5 = normal	Overall voice	Sustained /i/	Woo et al[134]	UC	○	○
Seven-point	1 = normal, 7 = very severely impaired	Overall voice	Counting and sustained /ah/	Adler et al[23]	●	●	○
	1 = normal, 7 = return in severity to patient's pretreatment level of SD or worse	Overall impression of voice normality/abnormality	Standard paragraph	Aronson and DeSanto[28]	○	○	○
	Unified Spasmodic Dysphonia Rating Scale◆ (Stewart et al.,[168]):	Overall severity, breathy voice quality, aphonia, voice tremor	UC	Blitzer et al[37]	UC	○	○
			UC	Blitzer et al[10]	UC	○	○
	1 = normal, 2 = mild, 3 = mild/moderate, 4 = moderate, 5 = moderate/severe, 6 = severe, 7 = very severe	Overall severity, strain/strangle voice quality, voice arrests	The Rainbow Passage	Tisch et al[122]	UC	○	○
	1 = normal/asymptomatic; 2 = mildly impaired; 3 = mildly/moderately impaired; 4 = moderately impaired; 5 = moderately/severely impaired; 6 = severely impaired; 7 = very severely impaired	Overall voice	Sustained phonation on /ah/ for 5 seconds, a single sentence from "The Rainbow Passage"	Damrose et al[50]	●	○	○
	1 = normal speech, 7 = most severe form of SD	Overall voice	Standard text of 92 words	Fritzell et al[64]	●	●	●
	1 = normal/none/efficient/natural, 7 = extreme/exceptional/excessive/inefficient/unnatural	Laryngeal tension, laryngeal tone, tremor in contextual speech, voice stoppages, intermittent strain-strangle, constant strain-strangle, loudness, pitch, vocal inflections, pitch breaks to higher pitches, rate, overall vocal efficiency, naturalness	The Rainbow Passage Spontaneous speech	Meyers and Anderson[93]	●	●	○
	1 = normal, 7 = severely impaired	Overall voice	The Rainbow Passage	Salvatore et al[109]	●	○	○
	1 = normal, 2 = mild, 3 = mild/moderate, 4 = moderate, 5 = moderate/severe, 6 = severe, 7 = extremely severe	Overall severity, strain-strangled voice quality, breathiness	Sustained /ah/	Zwirner et al[139]	●	●	●
Eight-point	Absolute preference judgment method: 0 = absence of quality; 7 = maximum perceived magnitude of quality	Overpressure (strain), aperiodicity (harshness/hoarseness), tremor, breathiness	Sustained phonation and The Rainbow Passage	Izdebski et al[74]	●	●	●
Eleven-point	0–10 scale, 0 = worst possible score, 10 = best possible score	Grade, Breathiness, Roughness (from GRBAS[170]) Intelligibility, Fluency, Voicing, Spasmodicity (from IINFVo[171]◆)	Standardized list of 40 German sentences	Dejonckere et al[53]	●	■	○
	−5 (breathy) to +5 (pressed)	Overall voice	2 seconds of sustained /ah/	Fisher et al[59]	●	●	●

• Yes; ○ No; □ Consensus ratings or mean scores used for data analysis; ◆ Developed and/or validated using a SD population.
Abbreviation: UC, unclear.

TABLE 9.
Clinician-Rated Visual Analogue Scales

Scale End Points	Parameters Evaluated	Stimulus	Reference	Blinded/ Randomized	Reliability		Comments
					Inter	Intra	
Percent normal function: 0% is inability to phonation, 100% is normal voice	Overall voice	UC	Blitzer and Brin[35] Blitzer and Brin[36]	○	■	○	Used in conjunction with percent of normal function as rated by patients. Most conservative score was used in data analysis.
0 = pervasive/extremely poor, 100 = absent/ extremely good	Overall voice quality, breathiness, roughness, brokenness, overall fluency, tension struggle, dysfluent syllables, vocal spasms	The Rainbow Passage	Cannito et al[44]	●	●	●	Custom-built VAS software was used to present stimuli and record listeners' responses.
0 = pervasive/extremely poor, 100 = absent/ extremely good	Overall voice quality, breathiness, roughness, brokenness.	The Rainbow Passage	Cannito et al[42]	●	●	○	Custom software, Visual Analog Scaling of Speaking Attributes was used to record responses.
0 = Normal, 100 = severely dysphonic	Overall voice	"Buy Bobby a puppy."	Dromey et al[54]	●	●	●	Ratings captured using custom Matlab routine
0 = normal voice, 1000 = worst possible SD	Overall voice	UC	Geneid et al[66]	●	●	●	Ratings made using VISOR program. Anchor voice samples with fixed scores provided as rating landmarks.
0 = bad/extremely pathological, 100 = good/normal	Overall grade (based on GRBAS)	Spontaneous speech	Langeveld et al[83]	UC	■	○	
0 = normal, 100 = extremely pathological	Extended GRBAS (Langeveld et al., 2000): grade, roughness, breathiness, asthenia, strain, aphonia, diplophonia, staccato, tremor, falsetto, vocal fry	UC	Langeveld et al[84]	UC	■	○	
0 = no change or absence, 100 = severe change or permanent presence	Degree of severity of vocal quality, strained-strangled voice quality, Oscillation of intensity, voice break, vocal tremor, roughness, breathiness, asthenia	Sustained /ah/	Rojas et al[105]	●	●	●	
0 = none, 100 = most severe/profound	Harshness, breathiness, tremor	20 sentences with high content of vowels to elicit AD SD symptoms, 20 sentences with high content of voiceless consonants to elicit AB SD symptoms.[169]	Rumbach et al[108]	●	○	○	

• Yes; ○ No; □ Consensus ratings or mean scores used for data analysis.
Abbreviations: UC, unclear; VISOR, Visual Sort and Rate.

from the day of treatment to document duration of treatment response, as well as information on adverse events (eg, breathiness, dysphagia, pain, dyspnea, stridor) were used by 10.4% (n = 13/125) of studies[12,35,36,39,40,62,78,88,90,91,104,121,140] and were counted as one type of outcome instrument. The magnitude of side effects was not objectively quantified. Two additional studies[85,114] required patients to complete ratings and/or diaries 1 week prior to and following treatment (range, 6 weeks−4 months ± 7 days). Of the studies using patient diaries, only Rhew et al[104] outlined a specific scale that patients used to rate their symptoms relative to pretreatment levels: −2 (much worse), −1 (worse), 0 (pretreatment level), +1 (better), and +2 (much better). Within the included 125 studies, ratings of patient satisfaction and voice outcome were also made exclusively posttreatment (eg,[23,25,27,33,72,78,86,90,104,110,115,119,120,123,127]). Although these measures are no doubt important, the absence of a pretreatment rating excludes these instruments from this study.

Measures used by listeners to rate vocal performance

Sixty-four studies reported outcomes based on perceptual rating conducted either by experienced/expert or naïve listeners. The measures by which experienced listeners rated vocal performance of patients with SD before and after treatment were highly variable. In total, there were 37 different iterations of ordinal and VASs (see Tables 8 and 9), with the stimuli and parameters evaluated varying widely between studies. Although some scales appeared to be commensurate with one another (eg, the Unified Spasmodic Dysphonia Rating Scale[168] used in Blitzer et al[10,37] and the seven-point rating scale used by Zwirner et al[139]), they were not cited as such and therefore, for the purposes of this study, have been counted as individual instruments. Of the available reliable perceptual scales, the grade, roughness, breathiness, asthenia, strain (GRBAS)[170] (in part or full), in both ordinal and VAS forms, was used in six studies (see Tables 8 and 9). Only one study by Dejonckere et al[53] utilized elements of the IINFVo rating scale[171] that was developed for use with substitution voice and has been proven as a robust measure for evaluating a SD population.[172] When using a VAS, 88.9% (n = 8/9) of studies required raters to judge voice samples against their own internal standards of normal. One study used anchor samples.[66] Scale end points were inconsistent across studies, with 0 indicating negative or positive depending on the study, complicating interpretation across studies (eg, Langeveld et al[83]—pathological to normal, and Langeveld et al[84]—normal to pathological).

Eight studies[33,34,61,80,81,106,108,115] relied on clinicians counting SD-characteristic voice breaks; however, only two[81,106] also spectrographically confirmed the presence/absence of breaks. Meyers and Anderson[93] reported the percentage of strained-strangled syllables during reading and spontaneous speech tasks, perceptually evaluating the frequency of occurrence of strained, squeezed, staccato, or effortful phonation. Paired pre-post comparison ratings of magnitude of improvement were presented in seven studies,[25,27,33,76,86,106,123] all of which used unique scales. Less commonly used methods of perceptual evaluation included the Mora method (ie, counting of impaired morae[19,73,99]), direct magnitude estimation of spasm and breathiness severity,[21,22] symptom checklists,[109] and percent word intelligibility.[30] Salvatore et al[109] used Aronson's[173] Voice Profile to provide a clinical characterization of phonatory and resonatory abilities before and after treatment. Kaszas et al[75] presented data using the Friedrich Dysphonia Index (FDI) but provided insufficient detail regarding the scale. Interpretation was further complicated as the original publication of the FDI is not available in English. Maronian et al[91] failed to outline the rating scale they used to evaluate strain, vocal breaks, and tremor. A voice profiling system was developed and published in Wilson et al[130]; however, results were reported descriptively.

Inexperienced or naïve listeners were used as raters in only four studies.[25,30,50,54] Allegretto et al[25] used 14 volunteers with no experience in evaluating voices to use paired comparison ratings, selecting the sample that represented the more pleasing or superior voice. Damrose et al[50] asked three volunteers to rate overall symptom severity using a seven-point scale, which was the same as that used by experienced judges (see Table 7). Dromey et al[54] used six graduate SLP students as novice raters, requiring them to complete perceptual analysis of symptoms to rate pretreatment and posttreatment SD severity; these students had been exposed to disordered voices but have not worked clinically with individuals with voice disorders. Similarly, Bender et al[30] used 30 graduate SLP students as listeners to rate speech intelligibility using a custom software package, the General List Delivery System.

DISCUSSION

In order to interpret research results, knowledge of how a successful outcome is defined and measured is critical. This study sought to identify (1) which outcome measurement instruments have been used to measure the effects of treatment in SD and (2) what constructs are measured by these instruments. A total of 220 different outcome instruments were identified. In addition to diversity in individual outcome measurement instruments, there was also an imbalance in the outcome constructs measured by the tools used in SD treatment research. Considered in reference to the WHO ICF, SD treatment outcomes were most often measured at a Body Function level (n = 212/220, 96%), supporting the notion that outcome measures in voice treatment are both prolific in number and narrow in scope. While it is important to measure outcomes at a Body Function level, it is equally important to measure outcomes more broadly. Research should measure outcomes that the "people representing the population of interest notice and care about (eg, survival, function, symptoms, health-related quality of life) and that inform an identified health decision"[174] (p. 26). Research should assist patients and clinicians to make decisions about issues that matter to them. As SD can be severely and chronically

disabling, multidimensional assessment that includes patient perceptions of treatment effect and impact is critical when analyzing the efficacy of therapy.

In reference to the outcome instruments identified in the current review, it is apparent that there is no unified approach to the measurement of outcomes in SD treatment research. Despite established methods of objective analysis being available, there appears to be no agreement as to what measures are most suitable for examining treatment effect in this population and how these measures should be collected. Furthermore, a major gap exists in terms of the measurement of standardized and validated measures of treatment satisfaction or patient perception of treatment impact. The use of patient-reported outcome measures in treatment trials is increasingly recommended.[175] Despite 77.5% (n = 62/125) of identified SD treatment studies incorporating some degree of patient-reported outcome measures (either subjective measures or those related to cognitive, psychosocial-emotional, or quality-of-life domains), the heterogeneity in the instruments used and their lack of validation for use within the SD population is an impediment to data analysis and synthesis.

The searches used within the current review did not include limits in terms of year of study publication. Accordingly, studies from as early as 1981 were included. Taking into account the advances in medical treatment for SD over the last few decades, it must be considered whether all of the outcome instruments used in earlier studies maintain relevance in contemporary research treatment. Furthermore, many of the instruments used in research were developed as clinical assessment tools, and further evaluation of their utility as research outcomes may be required. Ultimately, research should measure outcomes that reflect what "people representing the population of interest notice and care about (eg, survival, function, symptoms, health-related quality of life) and that inform an identified health decision"[174] (p. 26).

The current review did not include studies published in languages other than English, experimental studies, or studies that did not explicitly report both pretreatment and posttreatment measures; broader inclusion criteria would have likely further increased the already large number of outcome instruments identified. Furthermore, there is potential that despite the authors' best efforts to conduct thorough searches, some relevant articles may have been inadvertently missed. Although direct comparison across SD treatment modalities may be biased due to differing durations of follow-up (ie, follow-up duration is more likely to be less extensive after botulinum toxin therapy than after surgery), standardized objective and subjective outcome measures would provide valuable information regarding the effectiveness of interventions. It is possible that core outcome sets developed may need to be treatment dependent.

Future directions

To begin to develop a COS for use in SD treatment studies, international agreement must be reached regarding the outcomes of importance. A trilogy of stakeholder consensus studies examining perspectives of (1) people with SD and their communication partners, (2) researchers, and (3) clinicians working with people with SD will be completed using nominal group techniques and an international e-Delphi exercise. In order to generate a COS that satisfies all stakeholders, new tools for outcome measurement may require development and validation. Final agreement on a COS would be sought through an international consensus conference.

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