Down Syndrome Speech Intelligibility Diagnostic Treatment Study (DS-DxTx)

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Stand Alone Protocol – Down Syndrome Speech Intelligibility Diagnostic Treatment Study (DS-DxTx)

PI Name and Institutional Affiliation:

Houri K. Vorperian, Vocal Tract Development Lab, Waisman Center, University of Wisconsin-Madison

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Project Summary

This Down syndrome (DS) speech intelligibility diagnostic treatment study (DS-DxTx) is a clinical intervention study assessing the efficacy of a novel speech treatment approach for individuals with DS. DS is a common genetic disorder that causes lifelong intellectual disability where speech intelligibility is typically compromised affecting quality of life. The clinical management of communication disorders in individuals with DS is a priority for NIH's National Institute on Deafness and Other Communicative Disorder (NIDCD). The proposed treatment addresses the void in speech intervention and is based on the Vocal Tract Development Laboratory's (VTLab) research findings on anatomic, acoustic and perceptual studies from speakers with DS. Having identified specific difficulties in the production and perception of select vowels, this treatment focuses on accurate vowel production, while combining and adapting two established speech treatment approaches on articulatory accuracy and motor learning. Findings from this clinical intervention study are expected to pave the path towards optimal management of speech intelligibility in speakers with DS. Findings are also expected to provide the preliminary data needed to bridge the gap towards an exploratory clinical research proposal on functional anatomy as an intervention strategy.

Background and Significance

Down syndrome (DS) is a common genetic disorder that affects 1:691 live births each year in the United States. It usually results from three copies of chromosome 21 (trisomy 21) and causes lifelong intellectual disability where the average lifespan has doubled from 30 to 60 years. Speech intelligibility, an important indicator of communicative effectiveness, is typically compromised in DS. The ability to communicate is central to social interactions, and educational and vocational pursuits. Reduced speech intelligibility can severely limit the affected person's ability to enjoy full participation in these interactions and adversely affect quality of life. Few communication interventions are tailored to meet the needs of the Down syndrome behavior phenotype (Neil & Jones, 2018). However, to date, there is no evidence-based treatment guidance for DS (e.g., none listed in the Practice Portal of the American Speech-Language-Hearing Association) even though enhancing speech intelligibility, as a means to improve communication, is a high priority treatment goal that parents and others seek for individuals with DS. The goal of improved intelligibility through the lifespan is made all the more important given that the average lifespan for persons with DS has increased remarkably owing to improved health care. In fact, the 'clinical management of communication disorders throughout the lifespan in individuals with Down syndrome' is at the forefront of NIH-NIDCD's priorities.

The proposed DS diagnostic treatment study (DS-DxTx) addresses this void in speech intervention and is based on the culmination of research findings from the Vocal Tract Development Laboratory (VTLab) using anatomic, acoustic and perceptual studies in individuals with DS (with major findings summarized in the following paragraph). As noted above, currently there are no evidence-based speech treatment guidance for DS. The VTLab is in a unique position to address this deficit given research findings on the anatomic growth of craniofacial morphology in typically developing and atypically developing individuals (e.g. DS). Such comparisons permit understanding the role of typical and atypical functions (breathing, deglutition and speech) in shaping the anatomic structures in typically and atypically developing individuals during the course of development and across the lifespan (i.e. functional anatomy). In addition, the VTLab has examined the biological basis of speech development by examining anatomic-acoustic correlates using necessary equipment and established protocols to record

and analyze typical and disordered speech. The VTLab has also examined the acoustic-perceptual correlates of speech intelligibility in DS (NIH-NIDCD grants R01DC-006282 and DS-Administrative supplement). Given the research-backed knowledge that guides this clinical treatment study, we expect that the findings will help pave the path towards the ultimate clinical management strategies to improve speech intelligibility in individuals with DS.

As described below, this speech intelligibility diagnostic treatment study (DS-DxTx) is a clinical intervention study assessing the efficacy of a novel speech treatment approach using a combination of two established speech treatment approaches (on articulatory accuracy and motor control) while adapting them to produce low vowels when feasible. While both vowel and consonant errors contribute to reduced speech intelligibility (Bunton et al., 2007; Van Borsel, 1996; van Bysterveldt et al., 2010; Wild et al., 2018), commonly used tests of articulation generally do not provide for comprehensive assessment of vowel production (Eisenberg & Hitchcock, 2010), and subsequently most speech-language pathologists focus on consonant articulation errors (phonology) and do not directly address vowels in treatment. One of the important finding from the VTLab's speech perception/intelligibility research in DS (Wild et al., 2018) was that the low vowels /ɑ/ as in hot and /æ/ as in hat had a higher frequency of perceptual errors than the high vowels /i/ as in heat and /u/ as in hoot, particularly in males. Furthermore, another VTLab finding using acoustic analysis of all vowels with perceptual speech intelligibility ratings revealed that word-intelligibility improved when the production of the low vowels /ɑ/ and /æ/ had more distinctive second formants/vocal tract resonances (Vorperian et al., 2023 & 2019). Since these extreme vowels define the articulatory working space (i.e. space within the oral-pharyngeal cavity for the tongue to produce/articulate all the speech sounds), it was hypothesized that the smaller anterior facial skeleton in speakers with DS limited/compressed the tongue's front/back movements to distinctly produce the vowels /ɑ/ versus /æ/. Indeed, VTLab findings using anatomic measurements from medical imaging studies confirmed the smaller maxillary and mandibular measurements in DS (working manuscript). However, prior to entertaining a hypothesis that attribute the difficulty in low-vowel production to anatomic dysmorphologies, it was necessary to assess whether intensive treatment may play an important role in improving speech intelligibility. The proposed intervention is individualized and prioritizes the low vowels, yet also accounts for the multiple deficits (such as motoric, phonologic and hearing loss deficits) commonly present in individuals with DS. Therefore, as detailed below, the purpose of this study was to determine whether a treatment approach that focuses on the production of the low vowels, while combining and adapting two established treatment approaches on articulatory accuracy and motor learning, would improve speech intelligibility and more specifically the accuracy of vowel production in speakers with DS.

Findings are expected to pave the path towards optimal management of speech intelligibility in speakers with DS. Furthermore, the preliminary data from this clinical intervention study is expected to help bridge the gap towards advancing exploratory clinical trials addressing the role of upper airway functions on the developing anatomy in the oral and pharyngeal regions (functional anatomy).

Specific Aims/Study Objectives

The proposed project is an intervention study aimed at determining the efficacy of a novel diagnostic treatment plan addressing speech intelligibility in individuals with Down syndrome (DS) as a means to improve communication and subsequently quality of life. Speech intelligibility is often compromised in children and adults with DS and a lifelong problem for many individuals (Fawcett & Paralego, 2009; Kent

& Vorperian, 2013; Kumin, 1994). Therefore enhancing speech intelligibility is a high priority treatment goal that parents and others seek for individuals with DS. The speech impairment underlying the reduced intelligibility, however, is particularly challenging to assess and treat because it is potentially associated with multiple factors, including, but not limited to, craniofacial and laryngeal dysmorphologies (e.g. shorted midface skeleton; laryngomalacia), motor impairments (hypotonia, dysarthria, and apraxia), phonological delay or disorder, dysfluency, and hearing loss (Kent & Vorperian, 2013). Individually and in various combinations, these factors affect nearly every aspect of speech production to interfere with intelligibility (Kent et al., 2021).

The proposed intervention study to implement on individuals with DS, as described in the following section, is based on the natural evolution of research in the Vocal Tract Development Laboratory (VTLab) –as summarized in the previous section–. It is rooted in VTLab research findings from anatomic (working manuscript), acoustic (Vorperian et al., 2022 & 2019; Vorperian and Kent, 2014; Kent and Vorperian, 2013) and perceptual studies (Kent et al., 2021; Wild et al., 2018) on individuals with DS that the VTLab has been studying since 2000 with funding support from NIH-NIDCD. This proposed diagnostic treatment study (DS-DxTx) utilizes a holistic intervention approach that accounts for the likely motoric, phonologic and hearing loss deficits in individuals with DS. The smaller midfacial skeleton in individuals with DS has been hypothesized to cause crowding in the oral and pharyngeal cavities resulting in the disruption of all functions performed in the mouth and throat specifically respiration, deglutition and speech. Thus, a number of drastic surgical/medical interventions, such as tongue reduction, mandibular extraction and palatal expansion are commonly performed by medical professionals to address obstructive sleep apnea and drooling. **This study is expected to provide the data needed to assess treatment efficacy in improving speech intelligibility**; **also, to provide the preliminary data needed to clarify the extent to which craniofacial dysmorphologies affects reduced speech intelligibility**. The preliminary data from this study is expected to inform future clinical trials that examine the role of oro-pharyngeal functions, as an intervention strategy during early childhood, in the development of the anterior facial skeleton (functional anatomy).

Aim 1: Determine the efficacy of a newly devised intensive speech diagnostic treatment plan (DS-DxTx) that combines two established treatment approaches on articulatory accuracy and motor control (Cycles and the Script programs that are documented to be efficacious with other speech disorders) while predominantly using the low vowels as described below in the Methods section.

Speech intelligibility is hypothesized to improve as phonological errors decrease. Perceptual measures to assess treatment efficacy include: **(a)** the HAPP-3 score of Total Occurrence of Major Phonological Deviations (TOMPD score = Word/Syllable Structure Omission Sum (that includes omission and consonant clusters) + Consonant Category Deficiencies Sum); and **(b)** Percent Words & Multisyllabic words Correct (with tabulation of percent consonants correct and percent vowels correct).

Aim 2: Determine the extent to which craniofacial dysmorphology affects reduced speech intelligibility using a combination of perceptual and acoustic measures.

Accuracy in the perceptual identification of the low vowels (percent vowels correct) is hypothesized to remain unchanged if reduced accuracy is predominantly due to craniofacial dysmorphologies (underdeveloped/shorted midface skeleton). Perceptual measure will include percent accurate identification of the low vowels /ɑ/ versus /æ/ (% vowels correct) pre- versus post-treatment. Acoustic measure will include the first two resonant/formant frequencies of the vocal tract (F1 & F2) with

comparisons of pre- versus post- treatment acoustic measures (as well as VTLab TD normative values and DS acoustic data). Increased difference of the second resonant frequency (F2) for the low vowels /ɑ/ versus /æ/, related to the functional front/back movement of the tongue in the horizontal plane, combined with improved perceptual identification of the low vowels (percent vowels correct) will implicate the effectiveness of intensive treatment on low vowels using articulatory accuracy and motor control.

Research Design and Method

Approach

Participants with DS who speak English as their primary language will be recruited in this DS-DxTx study. Ten male speakers with DS ages 7 to 16 years will be enrolled in this study based on Wild et al. (2018) findings that males are less intelligible than females and that speech intelligibility improves up to age 16 years. Difficulty recruiting participants is not anticipated given available resources that we have used to recruit participants for former VTLab studies (Waisman Center's clinical and translational core, Goodnight Hall, and social media posts).

Procedures for DS-DxTx will entail formal intervention by a certified Speech-Language Pathologist and one assistant where each participant will receive an average of three hours of therapy/week over a 12 week period (36 required contact hours/participant), and 30 minutes weekly home practice using an app or flashcards/worksheets for therapy practice. Treatment will be in a quiet clinic room (location may include the Waisman Center, a local library/school, or GiGi's playhouse) with ongoing assessment of progress following ASHA best practice guidelines (ASHA, website March 13, 2018). All members involved in treatment will have HIPAA and CITI certification and be familiar with neglect/abuse and safety/security guidelines of vulnerable populations. They will also follow the universal cleaning precautions for all treatment and assessment materials. To ensure effective intervention, age appropriate activities and materials will be used during treatment while taking into account individual needs and interests.

The DS-DxTx study is rooted in Wild et al. (2018) findings that low vowels /ɑ/ as in 'hot' and /æ/as in 'hat' are less intelligible than the high vowels /i/ as in 'heat' and /u/ as in 'boot'. As described above, contrary to the common practice of targeting consonants in treatment, the proposed DS-DxTx will focus on low vowel accuracy. We expect that vowel accuracy will also impact accuracy of consonant production at the syllable level and help improve overall speech intelligibility despite the anatomic and/or motoric limitations present in individuals with DS. This DS-DxTx treatment combines two well established treatment approaches with documented treatment efficacy, the Cycles and the Script programs described below, and adapts both to using vowels, specifically the low vowels /ɑ/ and /æ/.

Each DS-DxTx session will include 40 minutes of the adapted Cycles program focusing on articulatory (phonological) training at the syllable/word level and 20 minutes of the adapted Script program for motor training at the sentence level. The adaptations are to ensure vowel-focused intervention to facilitate low vowel production stability with repeated practice. The Cycles phonological program is a treatment guidance for typically developing individuals with moderate to severe unintelligible speech (Hodson, 1992; Hodson, 2006; Hodson, 2011). The focus is on assessing and treating speech sound disorders in targeted patterns based on developmental phonology. The name 'Cycles' refers to periods where all phonological error patterns are facilitated in succession per target

phoneme (Hodson & Paden, 1991) with gradual increase in complexity per cycle. The program uses auditory bombardment (wearing personal amplification while hearing the target sounds), production drill and sound practice (i.e. repeating sounds, syllables, & words as practice) in facilitated context to yield accurate productions. The development phonological treatment is syllable units, consonant vowel (CV), VC, CVC or VCV, /s/ clusters and alveolars in words, then phrases. Currently, no efficacy data has been reported using the Cycles phonological treatment program with individuals with DS. However, individuals with DS often have moderate to severely unintelligible speech and a potential fluctuating history of otitis media (Hodson & Paden 1991). The Cycles design uses amplification and habituates accurate syllables through repeated practice which may assist with a fluctuating hearing loss and motor control planning (e.g.,apraxia, dysarthria). Modifications to Cycles specific to this treatment plan is the vowel-focused intervention that establishes distinct contrasts of the low vowels /ɑ/ and /æ/ that may result from anatomic and/or motor limitations. Facilitating low vowel stability while still following the targeted cycles of phonological intervention repeated practice adheres to the Cycles program design. Reducing the variability and automatizing productions of anticipatory sounds at the syllable level may improve co-articulatory effects of consonant accuracy in words. Priority of /ɑ/ and /æ/ vowels will supersede other vowel productions within each cycle of the treatment program.

The Script program is a motor training treatment guidance for typically developing individuals with acquired apraxia (Youmans, 2011; Wambaugh, et al., 2013) and those with cognitive disabilities (Kim, 1991; Goldstein, 1992). Script templates are common conversational topics with short phrase level productions that are practiced in unison, with prompting (fading unison), and then independently. Currently, no published data demonstrates the use of script training with individuals with DS. Our rationale for including script training for /ɑ/ and /æ/ vowel production is based on the instance theory of automation (Logan, 1988), and motor learning theory (Friedman, et al., 2010). The script (motor) training (Youmans, et al., 2011; Logan 1988) with visual support (Kumin, 2003) aims to improve the motor production/planning of vowels /ɑ/ and /æ/ in sentences while supporting the learning style of individuals with cognitive disabilities. Additionally, producing accurate and repetitive vowel + consonant productions with variable communication partners may aid generalization. Script topics choices will include a conversation starter, ordering at a restaurant, movie or video game (favorite parts) description, and/or how to invite a friend over. One script will be used per treatment session/visits to train the productions of /ɑ/ and /æ/ vowels in phrases. Once the vowels are mastered in the initial script, an additional one or two scripts may be chosen by participants and used as home practice. The /ɑ/ and /æ/vowel specific script is the same for all participants, additional scripts will follow the same template for blocked practice of phrases. The rationale for additional scripts is motivation to practice outside of treatment sessions and further generalization of intelligible speech with more practice. To ensure effective intervention, age appropriate activities and materials will be used during treatment while taking into account individual needs and interests.

Participants: Identification and recruitment

The following steps/criteria will be used:

Participants will include ten male participants with DS between the ages of 7-16 years old who want to improve their speech intelligibility.

Inclusion criteria: Participant eligibility criteria for this protocol, will be assessed by phone eligibility script (uploaded document titled “Phone screening form”) completed by parent/guardian to meet the following criteria:

- Males with a diagnosis of DS between the ages of 7 and 16 years, whose primary language is English, and who are interested in improving their speech intelligibility. All participants must consent/assent to participate.
- As this is a multiple single subject design study, services are available to all motivated participants who are willing to commit to the time/durations described in the diagnostic treatment.

During the phone interview the following information will be collected from participants:

- Date of birth, primary language is English, sex, date of birth (to confirm the subject's/participant's age and to ensure subjects/participants meet eligibility requirements), telephone, address, and/or e-mail address to contact the participant in case an appointment needs to be cancelled/rescheduled or the participant does not show up, cursory speech, language, orthodontia & hearing history, and medical conditions/health issues that may affect speech, language or hearing.

While consenting, all prospective participants will have the opportunity to 'agree' or 'not to agree' to the treatment plan.

Exclusion criteria: Individuals will be excluded if American English is not their primary language, they do not have Down syndrome, or are a female. Individuals who have a co-occurring diagnosis that affects communication abilities (e.g., diagnosed as deaf with cochlear implants, Autism, only use an AAC device to communicate) or a severe hearing loss which will limit their ability to participate in the treatment as described above will also be excluded. Individuals with a known mild or moderate hearing loss or current speech-language therapy services will not be excluded, but this information will be requested in the Parent Questionnaire as well as access to their current IEP.

Recruitment may occur from the following sources:

- Internet
- Newsletters
- Poster/ fliers

Internet recruitment may include web posts on social media pages of organizations, social media posts or online newsletters of community groups for families and specific to individuals with DS. This includes web postings of study flyers and brochures (on Waisman Center website, our lab's Website) and social media posts (see document called Social Media Recruitment Post) on social media pages of organizations (e.g. The Facebook page of Madison Area Down Syndrome Society (MADSS), GiGi's website).

The VTLab will distribute recruitment information in existing newsletters, both online and in print. The newsletters in which study information will be distributed will include those for parent and teacher organizations, private schools, public schools or vocational sites for persons with disabilities. Please see document called Newsletter Template.

The VTLab staff may provide recruitment materials at community informational or social events given prior approval from event organizers. If approval is given, a trained VTLab member(s) may also attend community social or informational events with recruitment materials, particularly those related to individuals with developmental disabilities including Waisman Center Day with the Experts, Madison Area Down Syndrome Society (MADSS) Buddy Walk, Special Olympics, Down Syndrome Association of Wisconsin (DSAW) events, and library story hours. Posters/fliers can be hung at locations including UW-Madison campus buildings, and select off-campus locations including other clinical research settings,

dissemination via other research labs, the Down Syndrome Clinics at the Waisman Center, and other community bulletin boards, local businesses, public libraries and public or private schools. Permission will be secured before posting in any of these buildings

While hanging paper/fliers in community locations, VTLab staff may stay briefly at the community location in order to answer questions related to the research study. When attending social and community events/locations VTLab staff may provide recruitment materials for those interested in more information. However, participants will not be screened or enrolled at these times, but rather instructed to contact our VTLab by phone or email. Participants will be recruited solely through their response to the VTLab approved recruitment materials.

Screening:

When potential subjects/participants contact the VTLab via e-mail, an e-mail template will be sent to them (see document titled Email response to interest in this study). No protected health information will be collected via e-mail and participants will be instructed to call the VTLab.

Potential Participant's parent/guardian will hear a Phone Script (Document: Phone Script) that describes the purpose of the DS-Diagnostic Treatment study. If they are interested in participating, then they will answer screening questions over the phone to determine eligibility, and to better prepare the testing room and VTLab personnel availability (Document: Phone Screening Form). The interview will consist of questions pertaining to the eligibility, the individual's health (e.g. hearing status), history of speech/language intervention, orthodontia history, any other health issues and willingness to participate in a 12-week treatment plan with a follow up post treatment assessment up to six-months later.

Measures: Baseline, Primary and Secondary Outcome Measures

All assessments, treatments and post treatment assessment will be performed by a certified Speech-Language Pathologist with an assistant present.

1. Following consent, an initial assessment will be completed to obtain baseline and primary outcome measures as follows:
    a. Current speech-language assessments (acoustic measures and language samples).
        i. An audio recording of words/sentences of VTLab Speech Production Protocol (#2016-1025) and a language sample will be made using a Shure microphone and recording onto a Marantz MPD 660. This recording procedure is identical to IRB Protocol # 2016-1025. In brief, recording will entail: ***a)*** repetition of a list of words and sentences, and ***b)*** a spontaneous language sample of 1-3 minutes where participant may answer a question or tell a story.
            a. Audio recordings will be used to assess treatment effectiveness via: ***i)*** acoustic analysis that entails making quantitative measurement of the speech signal including formant frequency measurements. ***ii)*** perceptual assessment by listeners to determine pre- post intelligibility score (% words correct, % consonants and vowels correct) comparison.
            b. Language samples will be used to determine Mean Length of Utterance (MLU). When the sample is suffiently lengthy, it will allow additional analyses that may include phonological calculation of the percent of consonants/vowels correct, token-to-token inconsistency measures, temporal measures, perceptual judgements of intelligibility by VTLab staff and/or naïve listeners, and consonant/vowel accuracy rating.

ii. Standardized speech-language testing (to personalize treatment and assess its efficacy):
    a. Hodson Assessment of Phonological Patterns, 3rd Edition [HAPP-3]
    b. Language test for expressive/receptive measures (Peabody Picture Vocabulary Test- PPVT)
    Scoring of standardized tests will be completed in the manner described by their publisher or as additional documents listed in this IRB (e.g, Parent Questionnaire).

b. Informal measures, questionnaire (speech-language history, current speech-language therapy/goals, family goals for speech intelligibility).
    i. Oral Motor Exam/ Motor assessment.
    ii. Intelligibility in Context Screening Form (ICS)
    iii. Parent Questionnaire

    Scoring of oral motor exam and ICS will be completed as specified by the publisher of assessment/form. The Parent/guardian Questionnaire(s) listed as additional documents in this IRB will be used as supplemental information to our formal assessment.

c. Current hearing status (e.g. participate in a hearing screening and/or provide a medical release for audiological records). A basic hearing screening will be completed, however, if a prior hearing loss exists then a medical release for the hearing record will be requested. The hearing screening is a standard procedure that entails detecting pure tones played over headphones or speakers to determine hearing acuity as an assessment that the participant can properly hear the stimuli and instructions. The American Speech Language Hearing Association criterion for passing a hearing screening is a pure tone average (PTA) from 1000, 2000, and 4000Hz that is better than 30dB HL in at both ears. If a participant fails the hearing screening, he may continue to participate in the study. The researcher will denote in the ANcoded file that the participant failed the hearing screening, as poor hearing may likely affect the participant's performance in the study in terms of following instructions and hearing stimuli &/or speech production may be altered if participant has a prolonged history of hearing loss. A participant who do not pass the hearing screening may ask for a copy of the results and will be referred to a professional audiologist with a strong recommendation for further testing.

d. The assessment phase to establish baseline data will be no more than three two-hour sessions (with breaks as needed).

e. Finally, for participants who currently receive speech-language treatment services (e.g, in school speech therapy), a release of information will be requested from the participant's family to provide a copy of their child's current school IEP and/or speech treatment goals. If the IEP addresses phonological interventions, we would request a copy of intervention targets from the treating speech language pathologist. This request will not be made from participants not enrolled in speech therapy services.

2. Each participate will participate in 12 weeks direct treatment of this diagnostic treatment program three times per week. Each participant will receive a total of 36 contact/treatment). Home practice of 30 mins/ week will be expected. Each treatment/intervention will entail:

    Auditory bombardment: a treatment that requires the participant to wear comfortable headphones, for a maximum duration of 10-15 minutes per hour session, while listening to speech sounds/words spoken at a low-level amplification to increase attention, sound awareness and discrimination.

Participate in Cycles and Script activities as described above. Therapy tasks may include games/activities that promote syllable, words and sentence repetitions to promote accurate productions. Age appropriate materials and reinforcements (e.g., stickers, stamps, praise, high fives) will be used to maintain motivation on speech tasks.

Complete homework tasks and 30 minutes weekly home practice. Homework activities will reinforce therapy goals and may be completed with paper activities or an app (per family preference).

3. *Post-Treatment Assessment* - Return at the conclusion of the 12-week treatment for a post-treatment assessment and again at approximately 1 month and 6 months post diagnostic treatment assessment. These visits will include a repetition of 3a., 3b., & 3c. in Current speech-language assessments above to determine the effectiveness of interventions at improving speech intelligibility.

   Assessment will include:

   a. Audio recording of repetition of lists of word/sentences and a language sample.
   b. Standardized speech language testing re-assessment with the HAAP-3.
   c. Informal measures and questionnaires that include:
      i. Oral Motor Exam/ Motor assessment.
      ii. Intelligibility in Context Screening Form (ICS)
      iii. Parent Questionnaire
   d. Hearing screening
   e. Post Treatment will be completed in the same locations as the Treatment phase and will include no more than 2, one or two hour sessions for each post treatment visit.

Privacy and Confidentiality:
Research studies will be conducted in private rooms and each participant's record will be kept confidential. Confidentiality will be maintained by assigning alpha-numeric codes to participants, and storing the study code key separately from the study datasets. Any data used in research reports, papers published in scientific journals, or presented at scientific meetings will be without names or identification numbers. Participant names will never be used in scientific presentations or publications.

The data from this study, including computer files, will be kept in a locked office (Waisman Center) and password protected computers and local servers using the alpha-numeric code that is assigned to each participant. Participants will never be referred to by name. The list of participant names and matching participant alpha-numeric code will be kept separate from datasets and in a confidential location that is available only to specific key-investigators involved in the study. All participants' audio speech/language recordings will be coded and stored on password protected computers. The raw data, such as waveform files and language samples, will be destroyed 7 years after the publication of our results in a peer-reviewed journal or a book. Dr. Vorperian (PI) will destroy identifiers at the end of the study.

Data and Safety Monitoring Plan

This diagnostic treatment study is a clinical intervention assessing the efficacy of a novel speech treatment designed to improve speech intelligibility in children with DS. All data acquired and/or

collected as well as measurements made are stored on secure and password protected network drives and VTLab computers using alphanumeric codes (details below in specific description section). All treatment members will have HIPAA and CITI certification and be familiar with neglect/abuse and safety/security guidelines of vulnerable populations. They will also follow the universal cleaning precautions for all treatment and assessment materials.

***Potential Benefits*:**
Speech-language perceptual and acoustic methods will be used to measure the effectiveness of this diagnostic treatment intervention on improving speech intelligibility in individuals with DS. This study can be used to determine the efficacy of this intervention strategy designed for individuals with DS. This information is significant for establishing data for speech treatment specific to individuals with DS that is a gap in current practice for speech language pathology. Additionally, improvement of clinical treatments may improve the quality of life of individuals with DS and may impact decision making on more drastic surgical interventions (e.g. mandibular distraction).

Potential psychosocial risks:
This study requires the individuals to participate in a novel treatment program that may not improve their speech intelligibility. Speech-language assessments will be completed with formal and informal measures. Participants and their guardians may request a copy of pre-, post- or pre/post assessments and treatment progress/goals. When this information is provided, the speech-language pathologist will schedule a meeting with the participant/family and provide descriptions of the results, goals, and treatment progress. Emphasis will be placed on ensuring that the speech-language testing information collected is understandable and any questions about speech intelligibility (e.g., improvement/no improvement) are answered.

Amplification of speech sounds requires listening to speech samples using comfortable headphones, which is a standard method in speech-language therapy. The hearing screening is similar, with the participant hearing a series of tones through comfortable headphones. No psychological stress is foreseen among participants being asked to undergo a hearing screening and or participate in amplification of speech sounds. The assessment portion of this study requires that the participant sit still during acoustic recordings and, some children may feel self-conscious speaking into a microphone.

As in all research studies, pose a small risk of breach of confidentiality with study records. This study is considered a minimal risk study and poses no serious risk to participants

***Potential physical risks*:**
There are no significant or major discomforts associated with speech recordings or participating in speech therapy activities. During hearing screenings/sound amplification some subjects may feel a slight discomfort from the pressure of wearing headphones.

***How risks will be minimized*:**
The findings are anticipated to demonstrate that vowel treatment is effective at improving speech intelligibility in males with Down syndrome, but we can't ensure that will be the case. In speech sound treatment it can be challenging to provide a control because withholding services may be considered unethical. In a recent study on effects of sound production treatment, change for treated items were larger than untreated items (Bailey et al. 2015). The Cycles and script programs have been effective with the typically developing population with acquired apraxia and individuals with cognitive deficits, for that reason, are unlikely to result in decreased intelligibility in the DS population.

To protect against and minimize potential risks, confidentiality will be maintained by storing data and records in secure, password protected computers in locked offices and cabinets (Waisman Center). Confidentiality will be maintained by assigning AN-Codes to subjects/participants, with the code keys being stored separately from the subject's/participant's study data (dataset). The code key will be stored in a password protected spreadsheet on password protected drives. Consent forms with participant/guardian signature will be stored in locked file cabinet the VTLab, Waisman Center, separate from the study dataset. Additionally, any electronic documentation that contains both AN-Code or personal health information will be password protected with restricted VTLab personnel access. Participant names will never be used in scientific presentations or publications. All individual audio recordings and language samples will be coded and stored on password protected computers on the Waisman Center and UW approved secure networks. Raw data, such as waveform files and language sample transcriptions of speech, will be permanently destroyed seven years after publication. Dr. Vorperian will destroy all HIPAA unique identifiers at the conclusion of this study.

In regards to participant visits, all equipment is cleaned/sterilized between participants. This includes headphones, toys (if used), microphones, flashcards, and all contact surfaces. When headphones are used the volume is monitored for participant comfort and safety. Water is also available and breaks are given when needed/requested.

***Explanation of risks in relation to anticipated benefits*:**
A documented and effective speech intervention program for individuals with DS may result in improved intelligibility and communication effectiveness, and guide efficacy in the field of speech language pathology. As stated above, the risks are minimal and prevention methods are in place. We do not anticipate any of the risks listed above to cause significant harm to participants. The anticipated benefits, on the other hand, are significant in that they assess the efficacy and advancement of an intervention strategies specific to improving speech intelligibility in individuals with DS.

Provisions to identify and address problems
The VTLab staff has taken preventative measures to eliminate unanticipated problems or potential complications and is in a position to resolve problems should any issues arise. In the unlikely case that unanticipated problems or complications arise, we will meet any unexpected medical emergency of our participants with appropriate response. All unanticipated problems or complications will be promptly reported to the IRB.

Should VTLab staff note any evidence of neglect or physical, emotional, sexual, or other abuse while conducting testing, we will as mandatory reporters, promptly report observations to the appropriate agency (e.g. Child Protective Services, Disability Rights Wisconsin).

Statistical Considerations

Analysis will entail using a multiple single-subject design (Byiers, 2012) where assessment of progress for each of the 10 male participants will be compared against himself. This is based on the expected variability in speech production across participants. Assessment measures will include: a) speech-language quantitative measures described below including phonetic transcription by a trained speech-language pathologist; b) acoustic measures; and c) perceptual measures for intelligibility score (percent correct) that the VTLab has been using and described in detail in Wild et al. (2018).

The VTLab Speech Production (IRB protocol 2016-1025) task includes the recording of words and sentences that participants produce, which are then analyzed acoustically using TF32 (Milenkovic, 2010) to measure the vowel formants; intelligibility is scored as percent correct (words, consonants, vowels) based on the transcription of lab staff and/or naïve listeners. For each participant, assessment will entail three pre-treatment baseline measures, and post-treatment measures at the completion of the 12-week treatment, and at one, and six months following completion of DS-DxTx. The initial assessment also will include standardized testing using the Hodson Assessment of Phonological Processes-3 to customize treatment plan, Peabody Picture Vocabulary Test, an oral motor exam, Intelligibility in Context Scale (ICS) questionnaire, parent questionnaires, and language samples to measure Mean Length of Utterance, and when sample is adequately length for intelligibility scoring.

Consultation with a statistician, available through Waisman Center core services, will be used.

Data and Record Keeping & Privacy and Confidentially:

Research will be conducted in private, quiet rooms and each participant's record will be kept confidential. Confidentiality will be maintained by assigning alpha-numeric codes to participants and storing the study key in a separate location from the study data. Subject/participant names will never be used in scientific presentations or publications. All subjects'/participants' audio speech/vocalization recordings will be coded and stored on password protected computers.

Each subject's/participant's record will be kept confidential. Any data used in research reports, papers published in scientific journals, or presented at scientific meetings will be without names or identification numbers. The data from this study, including computer files, will be kept in a locked office (Waisman Center) and password protected computers and local servers using the alpha-numeric code that is assigned to each subject/participant. Subjects/participants will never be referred to by name. The list of subject/participant names and matching subject/participant alpha-numeric code will be kept separate from datasets and in a confidential location that is available only to specific investigators involved in the study.

At the conclusion of study, findings of this diagnostic treatment study on speech intelligibility in individuals with DS will be shared at a conference and/or a peer reviewed journal.

Dr. Vorperian (PI) will permanently destroy all raw data, such as waveform files seven years after the publication of study results in a peer-reviewed journal or a book. In addition, all identifiers in the database are permanently destroyed at the end of the study.

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