STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

NCT03977701

Manipulating Linguistic Complexity to Improve Child Language Treatment Outcomes

DOCUMENT DATE: FEBRUARY 23, 2019

NOTE: THIS DOCUMENT REPLACES THE ORIGINAL WHICH WAS THE INCORRECT DOCUMENT UPLOADED TO THE SITE. THE DATE OF THE DOCUMENT REMAINS THE SAME.

OMB Number: 0925-000
Expiration Date: 03/31/2020

Validate XML & NIH Pre-Submission

* All mandatory data elements (fields/uploads) **on all screens** must be addressed in order to submit for NIH pre-submission validation.

Are Human Subjects Involved?	◉ Yes ○ No	(set on Setup Questions tab)
Is the Project Exempt from Federal regulations?	○ Yes ◉ No	(set on Other Project Information tab)
Exemption number:	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8	(set on Other Project Information tab)

If No to Human Subjects

Does the proposed research involve human specimens and/or data? Yes ○ No ○

If Yes, provide an explanation of why the application does not involve human subjects research. Add Attachment

Skip the rest of the PHS Human Subjects and Clinical Trials Information Form

If Yes to Human Subjects

Add an appropriate record for each proposed Human Subject Study

"Add New Study"

Or

"Add New Delayed Onset Study"

Delayed onset studies are those for which there is no well-defined plan for human subject involvement at the time of submission, per agency policies.

Attach file to **Other Requested Information** per funding announcement and/or agency-specific instructions.

Other Requested Information	**Original**	**PDF**

Add Attachment

Study Record: PHS Human Subjects and Clinical Trials Information

*** Always required field**

Section 1 - Basic Information

1.1. * Study Title (each study title must be unique)

Pho-Mo Complexity Intervention

1.2. * Is this Study Exempt from Federal Regulations? ☐ Yes ☑ No

1.3. Exemption Number ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8

1.4. * Clinical Trial Questionnaire

If the answers to all four questions below are yes, this study meets the definition of a Clinical Trial.

1.4.a. Does the study involve human participants? ☑ Yes ☐ No

1.4.b. Are the participants prospectively assigned to an intervention? ☑ Yes ☐ No

1.4.c. Is the study designed to evaluate the effect of the intervention on the participants? ☑ Yes ☐ No

1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome? ☑ Yes ☐ No

1.5. Provide the ClinicalTrials.gov Identifier (e.g., NCT87654321) for this trial, if applicable

Section 2 - Study Population Characteristics

2.1. Conditions or Focus of Study

Language Development Disorders Delete

2.2. Eligibility Criteria

Inclusionary Criteria

All participating children must meet the following inclusionary criteria:

- between the ages of 4 and 6 years of age;
- English monolingual;
- present with phonological disorder (PD, n = 12), developmental language disorder (DLD, n = 6), or co-occurring PD-DLD (n = 18) (see below for additional criteria for inclusion).

Participants will complete a battery of assessment measures. Information gleaned from these measures will be used to further determine eligibility for the proposed study, which include both quantitative and qualitative criteria.

In addition, all PD and PD-DLD participants must:

- exhibit 5 or more sounds in error across three or more speech sound manner classes,
- score less than or equal to 1.5 standard deviations below the mean on the Goldman-Fristoe Test of Articulation 3 (GFTA3), [135] and
- exhibit less than or equal to 20% accuracy on final consonants and clusters independent of tense morphemes.

Moreover, all DLD and PD-DLD participants must:

- score less than or equal to 1 standard deviation below the mean on the Preschool Language Scales - Fourth Edition (PLS-4), [136] a test of expressive and receptive language; and
- exhibit a mean length of utterance (MLU) less than or equal to 1 standard deviation below the mean for age- and demographic-matched peers, based on a language sample. [4]

Exclusionary Criteria

All participants must:

- not be receiving speech/language services elsewhere,
- pass a binaural hearing screening at 20dB,
- achieve score above a standard score of 70 on a test of nonverbal cognition (Leiter-R) [137], and
- have typical intellectual, hearing, social-emotional, and neurological development, per parent report.

In addition, to rule out concomitant difficulty in other domains of language all PD participants must:

- score > 1 standard deviation below the mean on the PLS-4 [136]
- have an MLU > 1 standard deviation below the mean for age- and demographic-matched peers, based on a language sample [4]

To rule out concomitant difficulty in phonology, the DLD participants must:

- score > 1.5 standard deviations below the mean on the GFTA3, [135] and
- exhibit fewer than 5 sounds in error and > 20% accuracy on final consonants and clusters independent of tense morphemes.

If the above criteria are not met, a child will be excluded from participation.

2.3. Age Limits **Minimum Age** 4 Years **Maximum Age** 6 Years

2.4. Inclusion of Women, Minorities, and Children Inclusion of women_m Delete Attachment

2.5. Recruitment and Retention Plan RECRUITMENT _ RE Delete Attachment

2.6. Recruitment Status Not yet recruiting

2.7. Study Timeline STUDY TIMELINE_Ba | Delete Attachment

2.8. Enrollment of First Subject 01-May-2019 | Anticipated

Inclusion Enrollment Report(s) Add Inclusion Enrollment Report | Remove Inclusion Enrollment Report

Section 3 - Protection and Monitoring Plans

3.1. Protection of Human Subjects PROTECTION OF HU | Delete Attachment

3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site?

☐ Yes ☑ No ☐ N/A

If yes, describe the single IRB plan Add Attachment

3.3. Data and Safety Monitoring Plan DATA _ SAFETY MON | Delete Attachment

3.4. Will a Data and Safety Monitoring Board be appointed for this study?

☑ Yes ☐ No

3.5. Overall Structure of the Study Team OVERALL STRUCTUF | Delete Attachment

Section 4 - Protocol Synopsis

4.1. Brief Summary

This proposed research program will evaluate the influence of morpho-phonological interaction in the language of children with phonological disorder (PD), those with developmental language disorder (DLD), and those children with co-occurring PD and DLD (PD-DLD) through manipulation of phonological and morphological complexity in the selection of treatment target words. Experiment 1

4.2. Study Design

4.2.a. Narrative Study Description

This proposed research program will evaluate the influence of morpho-phonological interaction in the language of children with phonological disorder (PD), those with developmental language disorder (DLD), and those children with co-occurring PD and DLD (PD-DLD) through manipulation of phonological and morphological complexity in the selection of treatment target words. Experiment 1

4.2.b. Primary Purpose Treatment

4.2.c. Interventions

Intervention Type	Behavioral (e.g., Psychotherapy, Lifestyle Counseling)
Name	Language Intervention
Description	The clinician will provide models, verbal and/or tactile cues, and/or conversational recasts of targeted linguistic forms (consonants, consonant clusters, morphemes) following the methodology of Gierut and colleagues (Experiment 1) and of Plante and colleagues (Experiment 2). A minimum of 50 (Experiment 2) and up to 100 (Experiment 1) productions will be targeted per 1-hour session.

Delete

4.2.d. Study Phase Phase 3

Is this an NIH-defined Phase III clinical trial? ☐ Yes ☑ No

4.2.e. Intervention Model Parallel

4.2.f. Masking

☑ Yes ☐ No

☐ Participant ☐ Care Provider ☐ Investigator ☑ Outcomes Assessor

4.2.g. Allocation Non-randomized

4.3. Outcome Measures

Name	Treatment Probe
Type	Primary
Time Frame	All participants will complete the Treatment Probe at the start of each treatment session. Maximum 18 sessions.
Description	The Treatment Probe is made of the selected treatment stimuli (verbs) that are consistent with the child's assigned experimental condition. These verbs have a final consonant or consonant clusters ("sees" vs. "seats"), and are mono- or bi-morphemic ("tease" vs. "sees"). Children will be asked to pronounce each word following presentation of a corresponding picture and a verbal prompt. The Treatment Probe allows us to track the effectiveness of treatment on the treated stimuli.

Delete

Name	Generalization Probe
Type	Primary

Delete

Time Frame	All participants will complete the Generalization Probe during baseline phase (minimum 3 times), after 9 treatment sessions, after the last treatment session, and 2
Description	The Generalization Probe consists of words and phrases that target each consonant, cluster, and morpho-syntactic constructs a minimum of 10 times across relevant contexts (i.e., word- and utterance-position). The Generalization Probe allows us to track the effects of treatment (generalization) to untreated stimuli and to monitor control variables.

4.4. Statistical Design and Power STATISTICAL DESIGI Delete Attachment

4.5. Subject Participation Duration 6 months

4.6. Will the study use an FDA-regulated intervention? ☐ Yes ☑ No

4.6.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/Investigational Device Exemption (IDE) status

Add Attachment

4.7. Dissemination Plan DISSEMINATION PLA Delete Attachment

Section 5 - Other Clinical Trial-related Attachments

5.1. Other Clinical Trial-related Attachments Add Attachment

Inclusion Enrollment Report

1. * Using an Existing Dataset or Resource ☐ Yes ☑ No

2. * Enrollment Location Type ☑ Domestic ☐ Foreign

3. Enrollment Country(ies)

USA: UNITED STATES Delete

4. Enrollment Location(s)

San Diego, CA

5. Comments

Planned

Racial Categories	Ethnic Categories				
	Not Hispanic or Latino		Hispanic or Latino		Total
	Female	Male	Female	Male	
American Indian/Alaska Native	1	1	1	1	4
Asian	1	1	0	0	2
Native Hawaiian or Other Pacific Islander	1	1	0	0	2
Black or African American	1	1	0	0	2
White	7	7	3	3	20
More than One Race	3	3	2	2	10
Total	14	14	6	6	40

Cumulative (Actual)

Racial Categories	Ethnic Categories									
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			Total
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native										
Asian										
Native Hawaiian or Other Pacific Islander										
Black or African American										
White										
More than One Race										
Unknown or Not Reported										
Total										

< Previous Report **Report 1 of 1** Next Report >

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INCLUSION OF WOMEN AND MINORITIES

Both male and female children will be recruited equally for this study. We expect that there will be an equal number of female and male participants within each group, as prevalence of PD, DLD, and PD-DLD is roughly comparable across females and males insofar as the number of participants that we plan to recruit is concerned.[138,139]

Phonological disorder and developmental language disorder affect individuals of all racial and ethnic backgrounds.[140] We do not exclude based on these criteria. Given the diversity of San Diego County, and in particular San Diego Unified School District, we are able to obtain participants from all ethnic groups. We will not exclude any participant on the basis of race or ethnicity.

INCLUSION OF CHILDREN

All participants will be children, ages 4 to 6 years. This age range represents a key time in language development and diagnosis of phonological disorder (PD) and developmental language disorder (DLD). The PI (Barlow) has conducted various treatment studies for children with PD. The Co-PI (Pruitt-Lord) is a clinically certified speech-language pathologist, specializing in enhancing clinical assessment, particularly for children with DLD. As such, the PI, Co-PI, and the research team have extensive experience conducting standardized and non-standardized language testing of children in this age range. In addition, all personnel working on this project have completed training in the protection of human subjects. The data will be collected within the labs and the university clinic that serve children and include facilities capable of accommodating children. The recruitment sites identified within San Diego Unified School District are sufficient to provide the targeted number of participants.

RECRUITMENT AND RETENTION PLAN

Recruitment:

The participants will be recruited through schools and community organizations but will not be enrolled in any other speech/language services elsewhere. Both male and female participants will be recruited, as will children from varied racial/ethnic backgrounds.

Participants will be recruited through long-standing collaborations with schools and community organizations in San Diego County (see Letters of Support from San Diego Unified School District [Taps Richard] and SDSU Speech-Language Clinic [Lopes]). Permission will be obtained from the school district and local school administrators before conducting recruitment efforts. Following protocol that has successfully been implemented in the past, we will provide teachers and parent groups at area preschools and community centers with information about the project. The study will be announced to prospective caregivers through informational packets (e.g., flyer, SDSU Institutional Review Board-approved parental consent forms, demographic questionnaire, envelope) sent home with the child.

Retention:

Incentives are set at a reasonable rate to cover time and travel, and will be staggered across each participant's enrollment. We will have a part-time clinical research associate devoted to recruitment and retention.

STUDY TIMELINE

	Year 1			**Year 2**	
	April	**May-Aug**	**Sep-Dec**	**Jan-Apr**	**May-Aug**
Activity	Recruitment starts (n = 36 participants) Continues through May of Year 2	9 participants for Summer clinic session	9 participants for Fall clinic session	9 participants for Spring clinic session	9 participants for Summer clinic session

PROTECTION OF HUMAN SUBJECTS

1. Risks to Human Subjects

a. Human Subjects Involvement, Characteristics, and Design:
The participants will include 36 English monolingual children between the ages of 4 and 6 years of age with phonological disorder (PD, n = 12), developmental language disorder (DLD, n = 6), or co-occurring PD-DLD (n = 18). The participants will be recruited through schools and community organizations but will not be enrolled in any other speech/language services elsewhere. All participants will have typical intellectual, hearing, social-emotional, and neurological development, per parent report. Both male and female participants will be recruited, as will children from varied racial/ethnic backgrounds.

Participants in all groups will complete a battery of assessment measures. Information gleaned from these measures will be used to further determine eligibility for the proposed study, which include both quantitative and qualitative criteria. Specifically, participating children must pass a binaural hearing screening at 20dB, and score above a standard score of 70 on a test of nonverbal cognition (Leiter-R).[137]

In addition, all PD and PD-DLD participants must exhibit 5 or more sounds in error across three or more speech sound manner classes based on performance on the *Protocol for the Assessment of English Phonotactics* (PEEP),[82,141] and must score ≤ 1.5 standard deviations below the mean on the *Goldman-Fristoe Test of Articulation 3* (GFTA3).[135] PD and PD-DLD participants also must exhibit ≤ 20% accuracy on final consonants and clusters independent of tense morphemes, based on performance on the PEEP.[141]

Moreover, all DLD and PD-DLD participants must score ≤ 1 standard deviation below the mean on the *Preschool Language Scales – Fourth Edition* (PLS-4), a test of expressive and receptive language.[136] DLD and PD-DLD participants also must exhibit a mean length of utterance (MLU) ≤ 1 standard deviation below the mean for age- and demographic-matched peers, based on a language sample.[4]

Finally, to rule out concomitant difficulty in other domains of language, PD participants must score > 1 standard deviation below the mean on the PLS-4,[136] and must have an MLU > 1 standard deviation below the mean for age- and demographic-matched peers, based on a language sample.[4] To rule out concomitant difficulty in phonology, the DLD participants must score > 1.5 standard deviations below the mean on the GFTA3[135] and exhibit fewer than 5 sounds in error and > 20% accuracy on final consonants and clusters independent of tense morphemes, based on performance on the PEEP.[141]

b. Study Procedures, Materials, and Potential Risks:
This study employs a single-subject, staggered multiple-baseline design. Data will include caregiver-reported demographic data, scores on the standardized tests, digital recordings of subjects' spontaneous language, treatment probes and generalization probes, computerized analyses of speech/language samples and probes, and transcribed responses from speech/language samples and probes. All such data will be collected following caregiver consent and child assent. Further, all data will be collected at the San Diego State University (SDSU) clinic, with the exception of the caregiver report, which may be completed by the caregiver at home.

Screening procedures will include administration of the following:

- Caregiver report of child history and language background,
- Binaural hearing screening,
- *Goldman-Fristoe Test of Articulation 3*,[135]
- *Preschool Language Scales – Fourth Edition* (PLS-4),[136]
- *Leiter-R*,[137]
- Spontaneous language sample, and
- *Protocol for the Assessment of English Phonotactics*.[141]

The proposed experiments will be conducted for research purposes only, and access to all data collected will be restricted to investigators and research assistants. Prior to accessing data, research assistants will be required to complete the Collaborative Institutional Training Initiative (CITI) Program.

Following these initial screening procedures, those children who meet the eligibility criteria above will be classified as having PD, DLD, or PD-DLD, per those criteria. They will then be assigned to a particular treatment condition (see Table 1). PD children will be assigned to one of four conditions of Experiment 1 (n=3 per condition) and DLD children will be assigned to one of two conditions of Experiment 2 (n=3 per

condition). PD-DLD children will be assigned to one of four conditions of Experiment 1 (n=3 per condition) *or* one of two conditions of Experiment 2 (n=3 per condition). Following treatment condition assignment, specific treatment target verb stimuli will be identified for each child.

The next set of procedures involve the following, with 1-hour sessions occurring three times weekly (see also *C.2.2. Experimental design*):

- Baseline testing phase, to include administration of the Generalization Probe (a minimum of three baseline sessions per child);
- Treatment phase (maximum 18 sessions), to include
    - Treatment Probe administered at the start of each session and
    - Generalization Probe collected after 9 treatment sessions;
- Post-treatment testing phase, to include Generalization Probe collected immediately following treatment, and at 2 weeks and 2 months posttreatment.

Following completion of the post-treatment testing, children will be dismissed from participation in the research program. Referrals, if needed, for further speech/language services will be provided.

The risks of the procedures associated with the proposed project are minimal and typical of children receiving speech/language services in the schools, with the exception that there is more testing involved, treatment occurs more frequently (three times per week as compared to 1 to 2 times per week in a typical school setting), and the procedures will occur at the university clinic. No individual testing or treatment session will last longer than 1 hour. Risks to the children may include boredom or fatigue. The children will also be informed that they can take breaks or permanently end any session.

Additionally, the frequent visits to the university for participation in the study may incur costs to participants' caregivers in terms of their time and transportation. For that reason, we will offer incentives for participation in the study.

2. Adequacy of Protection Against Risk

a. Informed Consent and Assent*:* To ensure voluntary participation, the caregivers of potential participants will be asked to return the consent forms in envelopes provided with the informational packet. The consent form will be written in culturally appropriate language that is straightforward and easy to understand. Copies of the signed consent forms will be returned to the caregivers with a reminder of how to contact the research program if they have any questions or concerns. Child assent will be obtained verbally before each session begins.

b. Protections Against Risk*:* Confidentiality will be maintained by assigning random subject identification numbers when consent forms are returned. This number will be used for all data analyses, testing information, and record keeping. The signed consent forms and list of names linked to the codes will be stored in a locked file cabinet only available to the principal investigators. The written and recorded data will be stored in a separate locked cabinet, available only to the research personnel directly involved in this study. Backups of the digital data will be stored on a password-protected server in the College of Health and Human Services at SDSU.

The risks of the proposed project to the children are minimal and do not exceed those that occur in everyday school life. Fatigue will be minimized by limiting the individual sessions to 1 hour and providing breaks as needed. Costs associated with time and travel will be offset by incentives provided to participants' caregivers.

c. Vulnerable Subjects: Because the purpose of the proposed study is to evaluate treatment target selection for children with PD and/or DLD, all participants will be children, ages 4 to 6 years. This age represents a key time in language development and diagnosis of PD and DLD. The PI (Barlow) has conducted various treatment studies for children with PD. The Co-PI (Pruitt-Lord) is a clinically certified speech-language pathologist, specializing in enhancing clinical assessment, particularly for children with DLD. As such, the PI, Co-PI, and the research team have extensive experience conducting standardized and non-standardized language testing of children in this age range. In addition, all personnel working on this project have completed the CITI training program in the protection of human subjects.

3. Potential Benefits of the Proposed Research to Human Subjects and Others

Potential benefits to participating children include speech, language, and hearing screening and treatment, as well as incentive payments given to caregivers as compensation for their time and transportation. The student research assistants will also gain valuable clinical and research skills through their involvement with this project.

4. Importance of the Knowledge to be Gained

The high-incidence disorders PD, DLD, and PD-DLD directly impact a child's ability to communicate and are among the most prevalent developmental disorders. The experiments proposed manipulate the complexity of treatment targets to identify the most efficacious treatment approaches for children who present with these disorders. Our proposal would reveal the nature of interactions between sound and structure in language for these children and will serve as the basis for future treatment studies that will allow children to benefit from treatment in less time than what has been shown to date.

DATA AND SAFETY MONITORING PLAN

The Data and Safety Monitoring Plan (DSMP) below will align with the policies and guidelines of the San Diego State University Human Research Protection Program, from which approval will be obtained prior to any recruitment of study participants begins.

Confidentiality

The study data will consist of digital recordings of children's speech, electronic transcripts of their utterances, and paper records (from study tests). All data will be viewed only by investigators and research assistants and will be entered into a database under password protection. All physical data files will be stored in protected locations and under lock and key except when being viewed by a member of the research team, and will not leave the Phonological Typologies and Child Language Development, Disorders and Disparities Labs. Four-digit participant IDs will replace individuals' names for all purposes, and therefore subject confidentiality will be maintained. Participants will never be identified by name in any publication or report.

Fidelity and Reliability

Periodic fidelity checks will be implemented by the PI, Co-PI, clinical research associate, or senior graduate research assistant to ensure that treatment protocols are administered consistently across participants. For the first 3 participants who enroll in each experiment, weekly checks will occur to verify that procedures and activities are uniform across sessions, and that all participants are given the opportunity to attempt approximately 96 productions per session. These checks will be based on observation of live sessions, review of recorded sessions, and data records. Fidelity checks with subsequent participants will occur during the first treatment week and then every 2 weeks in the same manner. For reliability, 20% of all pretreatment, baseline, treatment, and generalization data from each child will be re-transcribed and re-coded by a second judge (research assistant) trained in SALT,[4] Phon,[3] and IPA notation. Samples with reliability scores <85% will be re-transcribed and/or re-coded completely.

Data and Safety Monitoring Board

The Data and Safety Monitoring Board (DSMB) will consist of independent researchers at San Diego State University who conduct research with human subjects, including vulnerable populations (i.e., children, individuals with neurological impairment, the elderly), and who also engage in clinical research with individuals with communication disorders. They will monitor and evaluate study activities on a quarterly basis to ensure that the DSMP is being followed to the letter. This will entail observing clinical sessions with the study participants, inspection of the research facilities to ensure proper storage of confidential information, and verifying that fidelity and reliability checks are occurring as described above.

The procedures that will be used with the study participants are standard procedures used in current clinical practice. As they are behavioral in nature, they constitute low-risk trials. Further, the PI and Co-PI will not be blinded to the participants' assignments to study conditions, and therefore will be able to monitor all human subject interactions on a weekly, ongoing basis to ensure that the DSMP is being followed. Updates on this monitoring will be reported to the DMSB on a monthly basis.

Should any Adverse Events (AEs) or Unanticipated Problems (UPs) arise, they will be reported to the university Human Research Protection Program, following the guidelines delineated below. In addition, the PI will also report any such AE or UP to the NIDCD, the NIH Office of Biotechnology Activities and the Food and Drug Administration.

Stopping Rules

The study will be discontinued prior to completion in the event that the intervention procedures are directly associated with AEs, suggesting that the intervention is unsafe.

San Diego State University Adverse Event Reporting

The SDSU Human Research Protection Program's guidelines for reporting AEs and UPs are as follows [http://research.sdsu.edu/research_affairs/human_subjects/guidance]

A. Adverse Event and Unanticipated Problems Reporting
    1. Reportable Events/Problems
        a. All unanticipated problems involving risk
        b. Unanticipated Serious Adverse Events

Serious adverse events must be reported to the IRB immediately at least within 48 hours of the event. Serious adverse events are defined as(i) events that have resulted in death; (ii) are life threatening; iii) require inpatient hospitalization; (iv) result in persistent or significant disability/incapacity, (v) result in a congenital anomaly/birth defect; or (vi) any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse). All other problems (listed below) must be reported to the SDSU IRB within 5 days.

c. Any apparent serious and/or continuing non-compliance.
d. Protocol deviations
e. Any unauthorized use, disclosure, removal, theft, or loss of PHI or individually identifiable private information.

Examples of losses under item (e) above include but may not be limited to:

a. Signed consent forms, data collection forms or case report forms containing PHI
b. The loss or theft of a laptop, flash drive, smart phone or tablet containing private identifiable information.

B. How to Submit a Report of a Problem in Research

Please access the Adverse Event Report form on the HRPP website at: https://newscenter.sdsu.edu/researchaffairs/files/03111-SDSU_HRPP_Adverse_Event_Form.pdf and submit the form as an email attachment to irb@mail.sdsu.edu. For more information contact the HRPP office at 619-594-6622.

C. Review of a Report of a Problem in Research

The IRB will review the report to determine if the adverse event or problem is serious, unanticipated and related to the research. The IRB Chairperson will also determine if immediate action is warranted.

D. Convened IRB Review of a Report

When the IRB Chairperson determines the event is serious, unanticipated and related, the report will be reviewed at next IRB meeting. The Senior Research Affairs [IRB] Analyst will assign a primary reviewer to review and present the event at the meeting. The primary reviewer as well as all IRB members have access to the vIRB and are expected to review the report in prior to the meeting.

The IRB will consider the following actions:

1. Modification to the protocol
2. Modification of information in provided in the informed consent document and during participant consenting
3. Providing additional information to past study participants
4. Notification of current study participants if the new information might affect their willingness to continue participation
5. Requiring the re-consent of currently enrolled participants
6. Modification to the continuing review schedule
7. Monitoring of the research
8. Monitoring of the consent process
9. Suspension of research
10. Termination of research

E. For Cause Suspension or Termination of IRB Approval of Research

The IRB Chairperson or designee may require an immediate, temporary suspension of enrollment of new participants and/or continued participation of previously enrolled participants, pending convened IRB review of an adverse event, unanticipated problem involving risk or research that is not being conducted in accordance with IRB requirements.

Upon review, if the IRB determines there is an unanticipated problem involving risk, or that there is serious continuing non-compliance, they may vote to suspend or terminate approval of the research.

The IRB will notify the PI in writing of such suspensions or terminations. The correspondence will include a statement for the reasons for suspension or termination. The PI will be provided with an opportunity to respond to the IRB in person or in writing.

F. Mandatory Reporting to SDSU Institutional Officials and External Agencies

Reports of any suspension or termination of IRB approval will be promptly reported to the appropriate institutional officials, the HHS agency that supports the research, and OHRP. The reports will include the reasons for the IRB's action as well as:

1. The name of the institution(s) (e.g., university, hospital, foundation, school, etc.) conducting the research project;
2. The title of the research project and the title of any related grant, contract, or cooperative agreement;
3. The name of the principal investigator for the research project;
4. The number of the research project assigned by the IRB and the number of the applicable HHS award(s) (grant, contract, or cooperative agreement);
5. A detailed description of the reason for the suspension or termination; and
6. The actions the institution is taking or plans to take to address the suspension or termination (e.g., investigate alleged noncompliance, educate the investigator, educate all research staff, require monitoring of the investigator or the research project, etc.)

When an IRB (a) suspends or terminates its approval during the period for which IRB approval had already been given or (b) disapproves a research project at the time of continuing review, the IRB should establish procedures to ensure that the rights and welfare of currently enrolled subjects are protected, subjects are not put at risk, and subjects receive appropriate care, if indicated, during the period of suspension or following the cessation of the research. This is particularly important in the context of clinical trials. For example, the IRB, in consultation with the investigator and the subjects' treating physicians (if not the investigator), may need to determine whether it is in the best interests of currently enrolled subjects to (a) continue receiving the interventions that were being administered to subjects under the research project, (b) be transferred to another institution engaged in the research so that participation of the subjects in the research may continue, or (c) be transitioned to medical management outside of the research context. Continuation of subjects on interventions that were being administered under the research project may be appropriate at least temporarily, for example, when those interventions hold out the prospect of direct benefit to the subjects or when withholding those interventions poses increased risk to the subjects. If the IRB decides that already enrolled subjects should continue to receive the interventions that were being administered to subjects under the research project, data collection (especially safety information) should also continue for such subjects.

In the case of an adverse event or other research related problem, the IRB will determine whether the investigator has developed appropriate measures to remedy the problem and to avoid the occurrence of a similar problem in the future. If the IRB determines that the adverse event [or other problem] is related to the research and that the problem was unanticipated, the PI will be asked at a minimum to modify informed consent procedures so that current participants are notified of the event so that they may determine whether or not they wish to continue their participation. The investigator may also be required to revise the informed consent process for use with future participants so that all foreseeable risks that are involved in the study are described. In addition, the IRB will determine on a case-by-case basis whether additional substantive changes such as major revisions to the protocol are required.

Federal law may also require the IRB to report the incident to the Office of Human Research Protections (OHRP) (45 CFR 46.103(a)). The IRB will report the incident to OHRP when it has been determined that the adverse event is also considered an unanticipated problem and therefore meets all of the following criteria:

1. The adverse event is unexpected in nature, severity and frequency;
2. The adverse event is related or possibly related to participation in the research; and
3. The adverse event suggests that the research places subjects or others at greater risk of physical or psychological harm than was previously known or recognized.

(Modified from OHRP's "Algorithm for Determining Whether an Adverse Event is an Unanticipated Problem" available: http://www.hhs.gov/ohrp/policy/AdvEvntGuid.htm, p. 10).

Adverse events that do not meet the criteria as described above will not be reported to OHRP; however the SDSU IRB maintains that authority to require protocol revisions or suspend or terminate any protocol that is not being conducted in accordance with the SDSU IRB requirements for approved research or that has been associated with unexpected serious harm to subjects. The IRB will promptly notify the investigator if this determination is made.

G. Recognizing a Deviation from an IRB Approved Protocol

The IRB presumes the PI is implementing protocol procedures consistent with IRB approval. However, the IRB recognizes that deviations and exceptions to approved IRB protocols may occur. A protocol deviation occurs when there is inconsistency between the procedures carried out in a study and the procedures stated in the research protocol, or when regulations regarding the manner in which research is being conducted are not being followed. Protocol deviations may directly harm or present the risk of harm to human subjects, or may be administrative in nature, such as those related to data or record keeping. As indicated in section XI, protocol deviations should be reported to the IRB.

STATISTICAL DESIGN AND POWER

This study employs a single-subject, staggered, multiple-baseline design.[82,117-119] Consistent with this design, it includes a standard (minimum) number of subjects per study condition (n=3). Experiment 1 includes four different treatment conditions and two populations, and thus includes 24 participants (3 participants x 4 conditions x 2 populations). Experiment 2 includes two different treatment conditions and two populations, and thus includes 12 participants (3 participants x 2 conditions x 2 populations).

Consistent with the staggered MBL design, analyses will focus on individual performance. We will complete a visual inspection of accuracy data plotted over time for each child.[116,118,132] Level, slope, and variability of accuracy scores across all data points will be evaluated within and across children to compare different legs of the multiple baseline within and across treatment conditions for each experiment.[118,119,133] This type of individual case data allows us to examine individual differences in performance during and following treatment and is particularly meaningful to practicing speech-language pathologists.

In addition, clinically meaningful effect size will be determined by calculating the difference in mean accuracy across pretreatment probes and mean accuracy posttreatment divided by the standard deviation of accuracy post-treatment on the Generalization Probe.[73,116] Effect sizes obtained for each treatment condition in each experiment will be compared relative to one another, and to results from published studies reporting effect size.