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RESEARCH ARTICLE

Communication Bridge-2 randomized controlled trial: Recruitment and baseline features

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Abstract

INTRODUCTION: Non-pharmacological interventions may offer significant benefits to the quality of life for persons with primary progressive aphasia (PPA) and their care partners but have lacked efficacy trials. To help fill the efficacy gap, we provide the feasibility of recruitment, enrollment, randomization, and baseline data for the Communication Bridge-2 (CB2) randomized controlled trial (RCT).

METHODS: CB2 is the first international, single enrollment site, Phase 2, Stage 2, parallel-group, active control, RCT delivered via video chat to individuals with PPA and their care partners. Participants were recruited, screened, and randomized into one of two speech–language intervention arms.

RESULTS: Ninety-five participant dyads (PPA mean baseline age: 67.1; 48% female) from four countries were enrolled and randomized.

DISCUSSION: Global recruitment, enrollment, and randomization of individuals with PPA into a video chat–delivered non-pharmacologic RCT is feasible. This trial provides a potential model for conducting rigorous non-pharmacologic efficacy trials for Alzheimer's disease and related dementias.

KEYWORDS
Alzheimer's disease, behavioral intervention, frontotemporal dementia, non-pharmacologic intervention, primary progressive aphasia, speech and language therapy, superiority trial, telehealth

Highlights

- Primary progressive aphasia (PPA) negatively impacts communication participation.
- Communication Bridge-2 (CB2) is a telemedicine-delivered randomized controlled trial.
- CB2 included global recruitment and randomization of 95 PPA participant dyads.
- CB2, the first international superiority trial for PPA using video chat shows feasibility.

- The study provides a model for rigorous non-pharmacologic trials for Alzheimer's disease and related dementias.

1 | BACKGROUND

Language impairments (aphasia) with relative sparing of other cognitive and behavioral functions are the defining features of the clinical neurodegenerative dementia syndrome primary progressive aphasia (PPA).[1,2] The progressive loss of language negatively impacts communication and quality of life for persons living with PPA and their care partners, including shrinking social interactions and lowering participation in community activities.[3–6] Alzheimer's disease (AD) neuropathologic change or a form of frontotemporal lobar degeneration are the primary neurodegenerative diseases associated with PPA.[1,2,7] Current pharmacological approaches primarily target symptoms and have not shown efficacy for slowing, halting, or reversing the proteinopathies associated with PPA or related aphasic neurodegenerative dementia syndromes.[8–10] Non-pharmacological interventions, including speech–language and psychosocial interventions, have the potential to improve communication participation and communication confidence for persons with PPA and their care partners, which may positively impact overall quality of life.[8,11] However, rigorous randomized controlled trials (RCT) to guide clinical care practices have been absent.[8]

The Communication Bridge (CB) Research Program has been changing this landscape with strategically staged, rigorous clinical trials on a path toward implementation studies. The CB1 trial established the feasibility of delivering an intervention on a global scale using telehealth delivery and demonstrated gains in functional communication outcomes maintained 6 months postbaseline.[12,13] This report describes recruitment and baseline enrollment characteristics for the CB2 Trial. To our knowledge, it is the first superiority trial of speech–language intervention in PPA.

2 | METHODS

2.1 | Trial design

The CB2 clinical trial protocol was published previously, including rationale, clinical trial design, intervention, and assessment measures.[14] Briefly, CB2 is an international, single enrollment site (Northwestern University), Phase 2, Stage 2, randomized, parallel-group, active control, non-pharmacologic clinical trial delivered virtually within a telehealth service delivery model to individuals with PPA and their communication partners[14] (NCT03371706). All sessions were completed through video chat. The trial was designed to test whether the CB intervention is superior to the control arm intervention for improving (1) participation in everyday communication activities as measured by the Communicative Participation Item Bank (CPIB)[15] and communication participation goals using Goal Attainment Scaling (GAS)[16,17] and (2) self-reported communication confidence as measured by the Communication Confidence Rating Scale for Aphasia (CCRSA).[18,19] The secondary outcomes and the measures used to characterize the cohort were described previously and include accuracy for trained words and scripts.[14] Enrollment began in May 2018 and ended in April 2022. Outcomes from the full trial are expected in late 2024.

2.2 | Ethics approval

Informed consent was obtained from all participants and communication partners. The Northwestern University and University of Chicago Institutional Review Boards (IRBs) approved the trial. All consent procedures followed local IRB committee standards after IRB approval.

2.3 | Participants, eligibility criteria, outreach, and recruitment

Adult dyads, consisting of individuals with a clinical diagnosis of mild to moderate PPA and their communication partners, were enrolled in the trial. Detailed inclusion and exclusion criteria have been described previously.[14] Briefly, the clinical diagnosis of PPA was made by neurologists and supported by the available medical records.[1,2,20] A communication partner was defined as an informal caregiver (typically a family member or friend) who knew the participant with PPA for > 12 months; had close and regular contact with the participant; and provided emotional, communication, or activities of daily living support to the participant with PPA. All participants were required to self-report using English as their primary language, with adequate hearing and vision for communicating with others, and the ability to read functional materials.[14] Participants were also required to pass study-specific technology and speech–language therapy readiness screens outlined in the CB2 protocol publication.[14]

The trial intentionally enrolled participants from each of three recognized research subtypes of PPA—logopenic (PPA-L), agrammatic (PPA-G), and semantic (PPA-S)— which are differentiated by relative strengths and impairments in word finding, grammar, and semantics. Participants with PPA were assigned to PPA-L, PPA-G, or PPA-S groups following previously published criteria,[1,2,20] which were informed by screening and baseline assessment data as well as medical records provided by the participant.

Outreach, engagement, and recruitment of participant dyads occurred through digital marketing, direct clinician referral, outreach events, mailings, flyers, specialized support groups, educational presentations, postings on websites (e.g., Association for Frontotemporal Degeneration [AFTD], TrialMatch, FTD Disorders Registry, World FTD

United, the American Speech and Hearing Association, and ClinicalTrials.gov), self-referral, and earned media coverage. We actively sought opportunities to connect with clinicians across the world and those working with diverse communities.

2.4 | Interventions

The interventions were delivered by speech–language pathologists (SLPs) with a clinical master's degree and a Certificate of Clinical Competence issued by the American Speech-Language-Hearing Association. The components and protocol for the control and experimental arm interventions are described in the CB2 protocol publication.[14] An overview of the visit schedule is highlighted in Figure 1, in which both arms received two blocks of intervention followed by pre- and postassessments. This report is restricted to the baseline data. The experimental arm intervention, CB, is a multicomponent intervention aligned with a person-centered, participation-focused aphasia intervention framework. The control arm intervention is focused on improving underlying language impairments/processes and is aligned with an impairment-focused framework.

RESEARCH IN CONTEXT

1. **Systematic review**: The authors reviewed the literature using traditional sources (e.g., PubMed). The literature suggests that primarily non-pharmacological interventions have the potential to improve communication participation and communication confidence for persons with primary progressive aphasia (PPA) and their care partners, but have lacked efficacy trials. To help fill the efficacy gap, we provide the feasibility of recruitment, enrollment, randomization, and baseline data for the Communication Bridge-2 randomized controlled trial (RCT).
2. **Interpretation**: Results show global recruitment, enrollment, and randomization of individuals with PPA into a video chat–delivered non-pharmacologic RCT is feasible.
3. **Future directions**: This RCT provides a potential model for conducting rigorous non-pharmacologic efficacy trials for Alzheimer's disease and related dementias.

2.5 | Statistical considerations

2.5.1 | Determination of sample size and randomization

In the original power calculation, the target sample size was 90 participant dyads, with 36 in the control arm and 54 in the experimental arm. To account for a discontinuation rate over the follow-up period, the sample size used in the power calculation was 85 participant dyads, with 34 in the control arm and 51 in the experimental arm. There was 80% power at a two-tailed alpha = 0.05 to detect an effect size of 0.628 standard deviations. The power calculation was re-evaluated as part of the interim analysis. The final sample size was 95 participant dyads, 39 in the control arm and 56 in the experimental arm.

The protocol publication describes the randomization plan in detail.[14] Briefly, a permuted block randomization schedule was stratified by two trial interventionists and subtypes (semantic, agrammatic, logopenic) with a 3:2 ratio of experimental to control.

2.5.2 | Statistical analysis

The study arms were compared using descriptive statistics. Continuous variables were summarized using means, standard deviations (SDs), and ranges, and categorical variables were summarized using frequencies. The reporting of *p*-values for baseline group comparisons in randomized trials is not recommended in the Consolidated Standards of Reporting Trials (CONSORT) statement.[21] Effect sizes were calculated for baseline demographic and baseline primary outcomes to contextualize the relationships between the groups. For continuous variables, the effect size is Cohen *D*, the experiment – control group difference divided by a pooled SD. For categorical variables, the effect

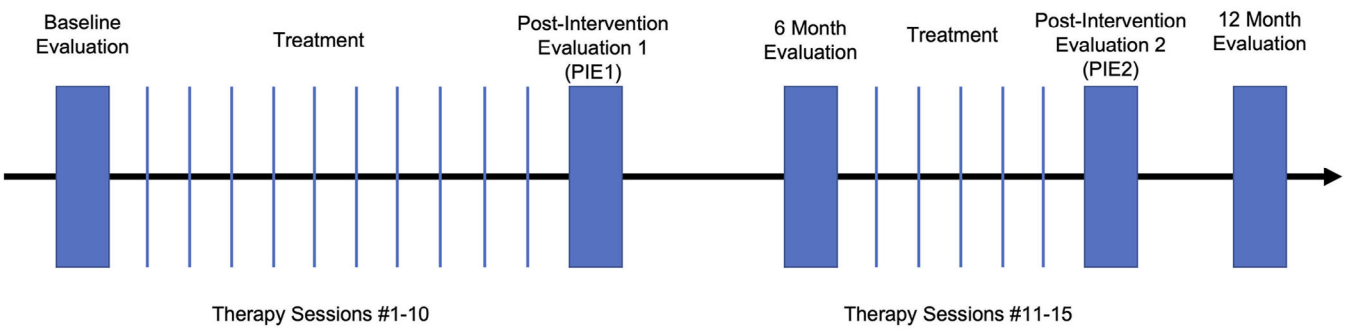

FIGURE 1 Overview of the intervention and evaluation schedule. Participants received 15 SLT intervention sessions and completed 5 evaluations (Evals) over approximately 12 months. SLT, speech–language therapy.

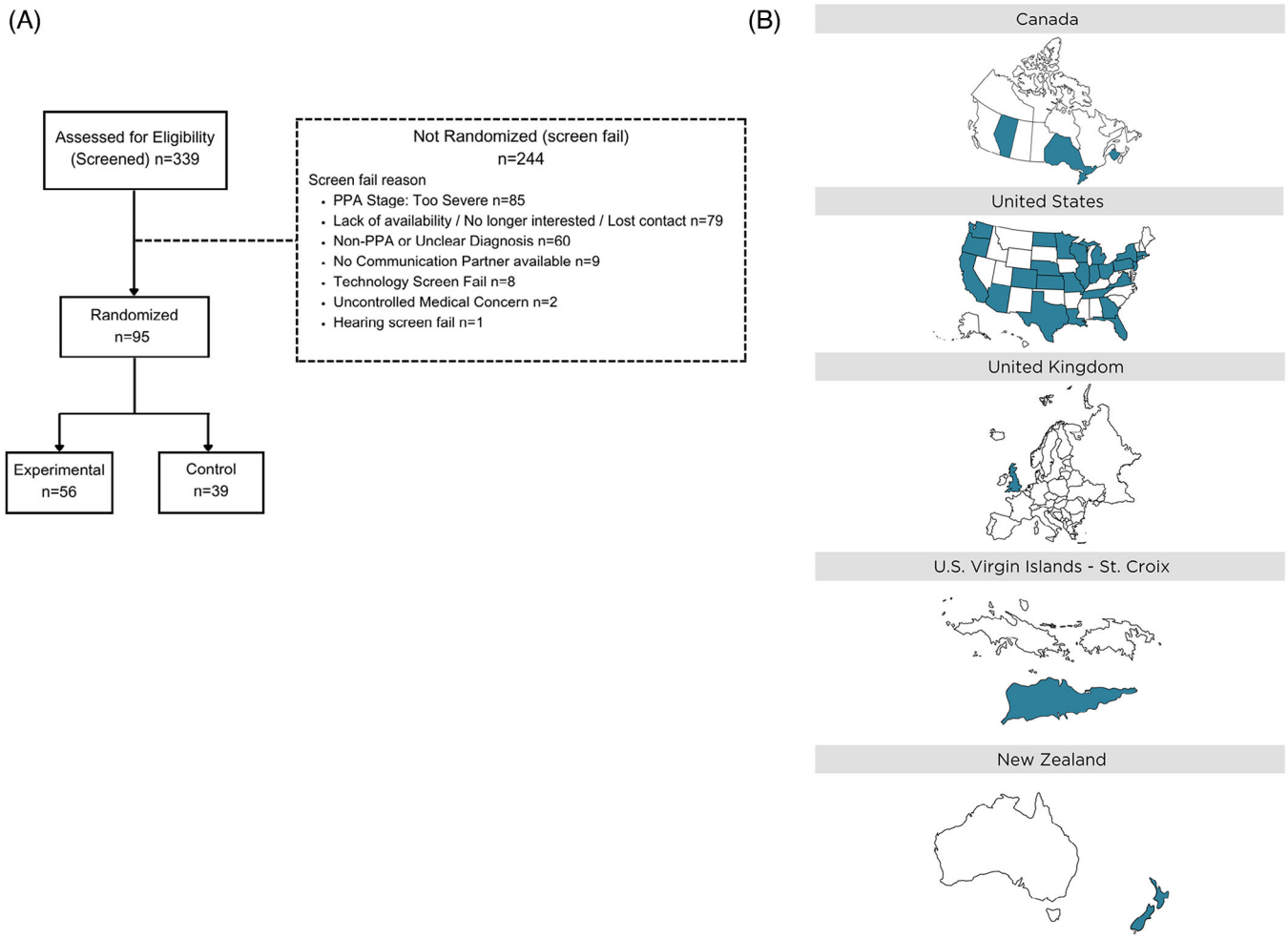

FIGURE 2 Flow diagram of the Communication Bridge-2 trial (A) and the global enrollment locations (B). PPA, primary progressive aphasia.

size is Cramer *V*, the square root of chi-square divided by the sample size. For randomized groups, effect sizes < 0.20 in absolute value are considered small.[22]

3 | RESULTS

3.1 | Study participants

A total of 339 participants were screened. Of these, 244 (72%) failed to enroll in the study. The three primary categories for screen failures included: (1) participant impairments too severe to meet inclusion criteria ($n = 85$), (2) inadequate availability or interest ($n = 79$), and (3) non-PPA or unclear diagnosis ($n = 60$; Figure 2A). Demographic information was available for a subset of the screen failures ($n = 144$). From this subset of data, the average age of persons who did not meet inclusion criteria was 68.1 years (range: 43.4–89.7), with 67 self-reported males and 77 self-reported females. Self-reported data revealed low racial and ethnic diversity, with the majority being White and non-Hispanic ($n = 116$), with 22 not reporting race, 5 Asian, 1 Black/African American, and one who did not report race but identified as Hispanic. Educational attainment was reported for 138 screen failures, with the majority having a bachelor's degree ($n = 52$), followed by a master's degree ($n = 33$). The remaining educational categories (high school/GED [$n = 19$], advanced graduate/PhD degree [$n = 18$], and some college [$n = 16$]) were similar among the screen failures.

Ninety-five participant dyads provided informed consent and were randomized into the trial. Demographic characteristics for the dyads are provided in Table 1. Participants with a diagnosis of PPA included 49 males and 46 females, with an average education of 16.4 years. Enrollment was global, coming from 25 US states, one US territory, 3 Canadian provinces, and four total countries (Figure 2B). Most participants were from urban areas ($n = 83$, 87.4%), as defined by the Federal Office of Rural Health Policy (FORHP) data files for the United States and the postal codes for Canada.[23] Participants from the three other countries were all considered urban based on their physical addresses. For the subset of participants (12.6%) who lived across two residences, the primary reported residence by the participant was used to determine urban versus rural settings.

Participants learned of the clinical trial through multiple sources. Ninety-three participants reported learning about the study from a single source. Eleven individuals indicated learning about the trial from

TABLE 1 Baseline demographic characteristics of the participants with a diagnosis of PPA and their care partners who were randomized to the trial.

Participants with PPA	All *n* = 95	Experimental *n* = 56	Control *n* = 39	Effect size
Age at onset, years,	63.4 +/– 7.6, (46–80)	63.1 +/– 7.4, (46–78)	63.8 +/– 7.9, (50–80)	–0.10
Age at enrollment, years	67.1 +/– 7.4, (52–82)	66.9 +/– 7.2, (53–81)	67.4 +/– 7.8, (52–82)	–0.07
Self-reported sex, male: female	49: 46	25:31	24:15	0.17
Self-reported race/ethnicity:				0.18
White, non-Hispanic/Latino	93	56	37	
White, Hispanic/Latino	1	0	1	
Asian, non-Hispanic/Latino	1	0	1	
Education, years	16.4 +/– 2.4, (12–21)	16.2 +/– 2.5, (12–21)	16.7 +/– 2.3, (12–21)	–0.22
Symptom duration, years	3.7 +/– 1.8, (0.4–8.6)	3.8 +/– 1.8 (0.4–8.4)	3.6 +/– 1.8, (1.3–8.6)	0.14
Prominent PPA subtype				
Agrammatic	26	15	11	
Logopenic	43	26	17	
Semantic	26	15	11	
Co-enrolled communication partners	**All** ***n* = 95**	**Experimental** ***n* = 56**	**Control** ***n* = 39**	**Effect size**
Age at enrollment, years	64.7 +/– 10.2, (26–90)	65.3 +/– 8.7, (40–90)	63.9 +/– 12.0, (26–78)	0.14
Self-reported sex, male: female	37:58	27:29	10:29	–0.23
Self-reported Race/ethnicity:				0.22
White, non-Hispanic/Latino	92	56	36	
White, Hispanic/Latino	1	0	1	
Asian, non-Hispanic/Latino	2	0	2	
Education, years	16.3 +/– 2.7, (10–26)	16.6 +/– 2.9, (12–26)	15.7 +/– 2.4, (10–21)	0.34

Note: Frequency or mean ± standard deviation, (range) are reported. For randomized groups, effect sizes < 0.20 in absolute value are considered small.
Abbreviation: PPA, primary progressive aphasia.

more than one source (10 participants with two referral sources and 1 participant with three referral sources). Of enrolled participants, clinician referrals were the most common source of referral into the trial (57 endorsements), with neurologists (36.8%) and SLPs (28%) as the most common referrers. Websites were the next most common referral source (26 endorsements), with various web-based sources of information, including our study-specific website, the Association for Frontotemporal Degeneration's website, and ClinicalTrials.gov. Additional referral sources included media (seven endorsements), word of mouth (four endorsements), referral from another research study (four endorsements), and support groups (four endorsements); four were unsure.

Participants represented each of the three subtypes of PPA; however, the PPA-L group enrolled at twice the rate of the PPA-G or PPA-S subtypes (Table 1). The randomization plan was stratified by subtype; therefore, recruiting equal numbers of participants for each subtype was unnecessary. Effect sizes (ES) for the baseline primary outcomes were low (i.e., < 0.20; CPIB ES: –0.17; CCRSA ES: 0.02). Symptom duration was similar across clinical trial arms. On average, aphasia severity was mild as measured by the Western Aphasia Battery Revised, with a mean Aphasia Quotient of 81.4 ± 8.4 (Table 2). The range data indicate a wider distribution of severity. Scores on the Activities of Daily Living Questionnaire (ADLQ),[24] designed to assess daily function in patients with dementia, were mild on average. Of the 95 participant dyads, 74 (78%) reported previously receiving speech–language therapy services (experimental: *n* = 42, 75%, control *n* = 32, 82%) before enrolling in the trial.

The demographics and relationship characteristics of the enrolled communication partners are provided in Tables 1 and 2. Most of the communication partners were female (*n* = 58, 61%). The vast majority were spouses or long-term partners (*n* = 84, 88%), while relatives (*n* = 5) and friends (*n* = 6) were similar in representation. The duration of the communication partner relationship of the dyad ranged from 5 to 64 years, with a mean of 38.4 ± 14.7 years. For most dyads, both participants lived at the same address (*n* = 85 dyads, 89.5%).

4 | DISCUSSION

The CB2 trial is the first global RCT for speech–language intervention for individuals with PPA. The trial successfully enrolled participants across each of the three subtypes of PPA (semantic, agrammatic, and

TABLE 2 Baseline outcome measurements and clinical and cognitive characteristics of the individuals with PPA and their communication partners.

Characteristics at baseline	All *n* = 95	Experimental *n* = 56	Control *n* = 39
Primary outcomes			
Communicative Participation Item Bank (CPIB)	46.5 +/− 6.3	46.0 +/− 6.1	47.1 +/− 6.5
Communication Confidence Rating Scale (CCRSA)	72.7 +/− 5.9	72. 6+/− 13.6	72.9 +/− 16.2
Goal Attainment Scaling (GAS)	0	0	0
Secondary outcomes			
% Accuracy trained words	54.3 +/− 24.7	60.7 +/−24.7	45.3 +/− 22.3
% Accuracy trained scripts	25.4 +/− 20.1	23.9 +/− 19.4	27.4 +/− 21.1
Assessments to characterize the PPA cohort			
Western Aphasia Battery-Aphasia Quotient (WAB-AQ):	81.4 +/− 8.4	81.4 +/− 8.0	81.4 +/− 9.1
Mini-Mental State Examination (MMSE)	23.4 +/− 5.2	23.5 +/− 5.2	23.2 +/− 5/4
Boston Naming Test (BNT)	36.3 +/− 18.5	37.1 +/− 18.3	35.2 +/− 19.0
Peabody Picture Vocabulary Test (PPVT)	29.8 +/− 6.8	29.9 +/− 6.9	29.8 +/− 6.6
Psycholinguistic assessment of language processing in aphasia (PALPA)—reading subtests (real & non-words)			
Non-words	6.7 +/− 2.4	6.8 +/− 2.3	6.4 +/− 2.5
Regular	9.3 +/− 1.5	9.3 +/− 1.6	9.3 +/− 1.5
Exceptional	8.3 +/− 2.2	8.5 +/− 2.3	8.1 +/− 2.1
Perception of Conversation Index-Dementia Alzheimer's Type (PCI-DAT): (Possible maximum)			
Conversational difficulties (154)	41.3 +/− 22.4	40.7 +/− 23.3	42.1 +/− 21.3
Actions you use (168)	83.1 +/− 25.7	82.6 +/− 25.6	83.8 +/− 26.2
Actions your relatives use (84)	34.2 +/− 10.3	33.7 +/− 9.2	34.8 +/− 11.7
Feelings (56)	20.5 +/− 11.7	21.1 +/− 11.3	19.7 +/− 12.5
Challenges (56)	16.2 +/− 12.2	17.6 +/− 12.9	14.2 +/− 10.9
Communicative Effectiveness Index (CETI)	72.0 +/− 17.4	73.1 +/− 18.9	70.4 +/− 15.2
Number of communication modalities used by participants, Social Networks Inventory (SNI)^{M}	7.8 +/− 1.2	7.6 +/− 1.2	8.2 +/− 1.2
Health Utilities Index (HUI)			
HUI 2	0.82 +/− 0.09	0.82 +/− 0.09	0.82 +/− 0.08
HUI 3	0.71 +/− 0.20	0.69 +/− 0.22	0.72 +/− 0.18
Activities of Daily Living Questionnaire (ADLQ)	14.9 +/− 10.0	15.6 +/− 11.1	13.8 +/− 8.3
Assessment for Living with Aphasia	61.8 +/− 9.9	62.1 +/− 9.9	61.3 +/− 10.2
PROMIS Anxiety	49.8 +/− 6.4	49.0 +/− 5.7	51.0 +/− 7.1
PROMIS Depression	50.5 +/− 7.8	50.2 +/− 7.6	50.9 +/− 8.1
Neuropsychiatric Inventory–Questionnaire (NPI-Q), total number of symptoms	1.9 +/− 2.0	2.0 +/− 2.1	1.7 +/− 1.8
Rivermead Behavioral Memory Test	8.1 +/− 2.3	8.3 +/− 2.5	8.0 +/− 2.2
Assessments to characterize the communication partners			
PROMIS Anxiety	50.1 +/− 6.7	50.4 +/− 6.8	49.7 +/− 6.6
PROMIS Depression	48.0 +/− 6.2	48.5 +/− 5.8	47.3 +/− 6.7
Montgomery Burden Interview (MBI), Stress	1.8 +/− 0.6	1.8 +/− 0.6	1.8 +/− 0.7
MBI, relationship	1.2 +/− 0.4	1.2 +/− 0.4	1.2 +/− 0.5
MBI, objective	1.6 +/− 0.7	1.6 +/− 0.7	1.5 +/− 0.6
Characterization of dyadic relationship			

(Continues)

TABLE 2 (Continued)

Characteristics at baseline	All *n* = 95	Experimental *n* = 56	Control *n* = 39
Relationship to person with PPA, *n*			
Spouse	81	48	33
Friend/neighbor	6	5	1
Child	4	1	3
Partner	3	2	1
Sibling	1	0	1
Years of relationship	38.4 +/− 14.7, (5–64)	37.5 +/− 13.8, (5–64)	39.5 +/− 15.9, (7–63)
Lives at the same address	Yes: 85 No: 10	Yes: 50, No: 6	Yes: 35, No: 4
Revised Dyadic Adjustment Scale (if CP is a spouse or partner)	*n* = 85	*n* = 51	*n* = 34
Total score	54.3 +/− 5.8	55.0 +/− 5.9	53.3 +/− 5.7
Parent-adult child questionnaire (PACQ-M, if CP is an adult child, sibling, friend, or neighbor)	*n* = 10	*n* = 5	*n* = 5
Regard (possible range 0–3)	2.46 +/− 0.45	1.97 +/− 0.64	2.64 +/− 0.22
Responsibility (possible range 0–3)	1.04 +/− 0.68	1.05 +/− 0.60	1.03 +/− 0.83

Abbreviations: CP, communication partner; PPA, primary progressive aphasia; PROMIS®, Patient-Reported Outcomes Measurement Information System.
[a]Study adapted version. NPI-Q Total Score: The total score represents the sum of all endorsed symptoms. Participant-centered GAS goals are developed during the baseline evaluation sessions. Each GAS goal is written such that the current level of function/performance is anchored at '0'. Discourse samples were also collected at baseline but do not have a simple summary score that could be provided here.

logopenic). The baseline data reported here show that remote enrollment and assessment of clinical and cognitive features of those living with PPA and their communication partners is feasible, which is vital for designing future trials, including eventual pragmatic trials, implementation, and dissemination.[25] Accessing clinicians knowledgeable about PPA has been cited as a barrier;[11,12] however, the feasibility of telemedicine enrollment demonstrated in the CB2 trial offers one potential solution to improve care accessibility.[12]

With 95 participant dyads, the CB2 trial represents the most extensive study of PPA intervention to date and provides important data for planning future large-scale efficacy, effectiveness, and pragmatic trials. A recent systematic review initiated in part by the Academy of Neurologic Communication Disorders and Sciences (ANCDS) highlights this prior gap. Of the 103 studies identified (between 1994 and May 31, 2021), 88.2% had samples of ≤ 5 participants. Most (84.2%) used single-subject designs, and none were RCTs. The National Institutes of Health (NIH) Stage Model for Behavioral Intervention Development provides a robust structure for developing maximally potent and implementable interventions.[26] Using the NIH Stage Model as a classification guide, previous PPA intervention studies primarily align with Stage 0 and Stage 1 and offer limited insight into generalizability and implementation, especially given the known heterogeneity in initial symptoms, the emergence of new symptoms, and the pace of decline in PPA.[27–33] The CB2 trial design assesses efficacy in a research setting, consistent with Stage 2. The multicomponent and person-centered design of the CB2 experimental arm and the relatively large enrollment size of the CB2 RCT assist in filling critical gaps in the level of evidence and in addressing aspects of generalizability relevant to implementation and dissemination.

The CB2 trial includes systematic demographic, clinical, cognitive, communication, and relationship assessments from the participating dyad, which promotes reproducibility. These data will also allow for the examination of potential mediators, moderators, and other factors associated with the primary and secondary trial outcomes.

The CB2 trial represents a significant shift in moving beyond impairment-based measures to focus on what matters most to people and families living with PPA.[34] The primary and secondary outcomes of the CB2 trial assess communication participation, communication confidence, and direct measures of naming and fluency, which allows for an appraisal of the impact of the intervention across multiple aspects of language and quality of life. These outcomes are aligned with word-finding being a nearly universal and early feature of PPA[7] and the negative impact that PPA has on communication, daily activities, and quality of life.[4,5] In contrast, the recent systematic review shows the assessment of naming/lexical retrieval (commonly to standard word lists) was the most reported target (65% of the studies), while quality of life and functional communication were rarely targeted (6.8%).[8] The CB2 outcomes are also consistent with US Food and Drug Administration requirements that interventions should incorporate functional and meaningful outcomes.[35]

This study successfully enrolled participants with mild-to-moderate PPA. The ability to enroll individuals at relatively mild stages has historically been challenging, partially because of the low awareness of the syndrome among the community and medical professionals, which has

negatively impacted the efficiency of the diagnostic process. It commonly takes years rather than months to obtain a diagnosis. Over the past decade, there has been an increase in disease awareness of PPA propelled in part by prominent efforts from non-governmental organizations (e.g., The Association of Frontotemporal Degeneration, World FTD United), and increased funding for AD and related dementias research. These developments likely positively impacted enrollment for the CB2 trial; however, recruitment was still laborious and required broad, multifaceted efforts. Clinician referrals and websites were the most endorsed referral sources, signifying the importance of increasing outreach for these less common syndromes. However, the large number of screen failures related to severity, unclear diagnosis, or a diagnosis of another related neurodegenerative syndrome (i.e., PPA+, prominent aphasia with dementia, primary progressive apraxia of speech, AD dementia with prominent aphasia) highlights an unmet need for care across the continuum of the disease. Consistent with many observational and intervention reports, enrolled participants with a diagnosis of PPA were in their mid-60s and college educated. Enrollment of logopenic participants outnumbered enrollment of the other two subtypes. In reviewing our engagement efforts, screening data, and enrollment data, there were no obvious systematic biases in recruitment sources or efforts, participant demographics, or other features that would account for greater enrollment of PPA-L participants. Most of the communication partners were spouses. Although enrollment spanned four countries, racial and ethnic diversity was low, which is a known area of challenge in PPA with many potential contributors, including low disease awareness in diverse communities and practical design constraints (e.g., inclusion criteria that required English as the primary language). The CB2 trial used several strategies to raise awareness, provide education, and support recruitment into the trial including digital marketing, direct clinician outreach to specialists and non-specialists, hosting educational conferences, and presentations at scientific and community events. Building relationships and awareness requires time, consistency, and resources. Multifaceted and intentionally planned outreach, recruitment, and retention plans are essential for increasing disease awareness and diversity participation in the future. Part of the enrollment for this trial occurred during the Covid-19 pandemic. The pace of enrollment was negatively impacted during this period. Despite this challenge, the enrollment goals were met, in part, because of the telehealth model.

In conclusion, this report highlights important proof of concept feasibility for global enrollment of persons with PPA and their care partners into a relatively large telemedicine-based (video chat) RCT. Such feasibility is vital for the development and planning of future trials and for establishing evidence-based best practices for intervention for those living with PPA and related dementias.

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CONFLICT OF INTEREST STATEMENT

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CONSENT STATEMENTS

The authors have reviewed and approved the submission of this manuscript. Informed consent was obtained from all human participants prior to trial enrollment.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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