


# Primary Progressive Aphasia:



## Clinical Features & Intervention Opportunities

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 The University of Chicago

**Nothing to disclose**

**NIH Funding:** R01NS075075, R01AG056258, R01AG051425, R01AG077444, R01DC008552, P30AG13854, P30AG072977



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# The Healthy Aging & Alzheimer's Research Care (HAARC) Center



**HAARC Registry**  
PPA Observational studies

**communication BRIDGE**

**ADNI**  
Alzheimer's Disease Neuroimaging Initiative

**Super.Aging**  
RESEARCH INITIATIVE

**New studies...**




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# Definitions for dementia over time

**1900s**

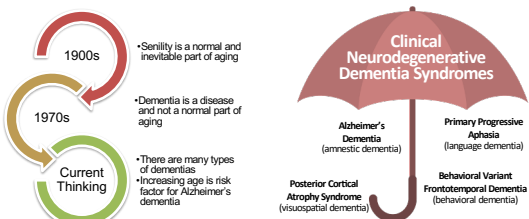
- Senility is a normal and inevitable part of aging



**1970s**

- Dementia is a disease and not a normal part of aging

**Current Thinking**

- There are many types of dementias
- Increasing age is risk factor for Alzheimer's dementia



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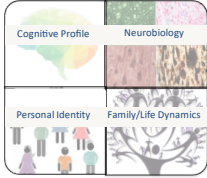
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### Multidisciplinary Aging & Dementia Investigations

Investigated through multiple perspectives, supported by several integrated programs



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### Primary

*Impairment is prominent in a single domain (language) with relative sparing of other domains early on (e.g., memory, personality and perception)*

### Progressive

*The impairment will get worse over time, since it is caused by a neurodegenerative disease*

### Aphasia

*a language impairment*

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McDaniel, 2001, 2003, 2009

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### How is the diagnosis of PPA made?

Ruling in and Ruling out

- Medical history from client & family
- Neurological exam
- Neuropsychological assessment
- Laboratory Measures\*
  - Including blood-based and imaging biomarkers



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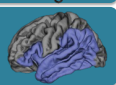

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### Fundamental features of PPA

<b>Symptoms</b> (Clinical Syndrome)	PPA: Progressive aphasia with relative sparing of other thinking abilities	
<b>Location in the brain</b> (Neuroanatomy)	Relatively focal atrophy (brain cell loss) within language parts of the brain	
<b>Disease</b> (Neuropathology)	<del>PPA disease</del>	

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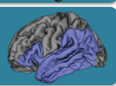
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### Fundamental features of PPA


<b>Symptoms</b> (Clinical Syndrome)	PPA: Progressive aphasia with relative sparing of other thinking abilities	
<b>Location in the brain</b> (Neuroanatomy)	Relatively focal atrophy (brain cell loss) within language parts of the brain	
<b>Disease</b> (Neuropathology)	There are 3 families of neuropathology that can cause PPA	

Family 1




Alzheimer's disease

Family 2



Frontotemporal lobar degeneration (FTLD-TAU)

Family 3



Frontotemporal lobar degeneration (FTLD-TDP43)

Emerging field:  
In vivo biomarkers to detect contributing proteinopathies at the individual level

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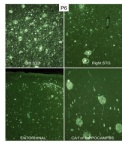
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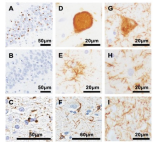
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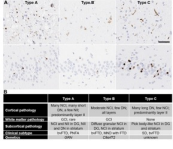
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### Fundamental features of PPA

<b>Family 1</b> Alzheimer's disease (Aβ + NFT)	<b>Family 2</b> Frontotemporal lobar degeneration (FTLD-TAU) Picks (3 repeat tauopathy)    CBD/PSP (4 repeat tauopathy)	<b>Family 3</b> Frontotemporal lobar degeneration (FTLD-TDP43) Forms A-E
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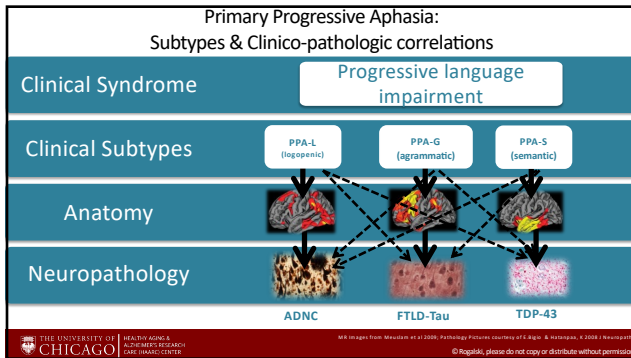
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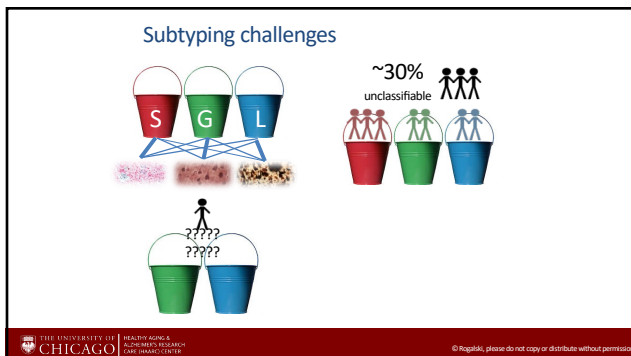
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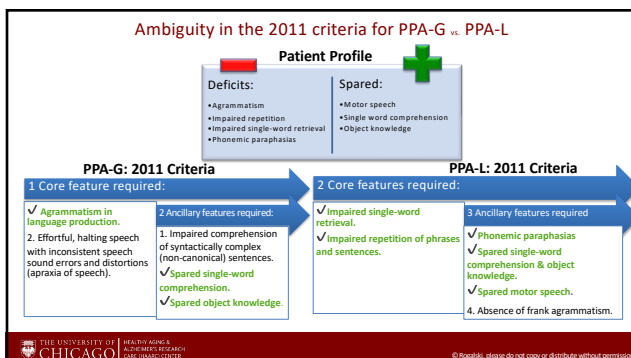
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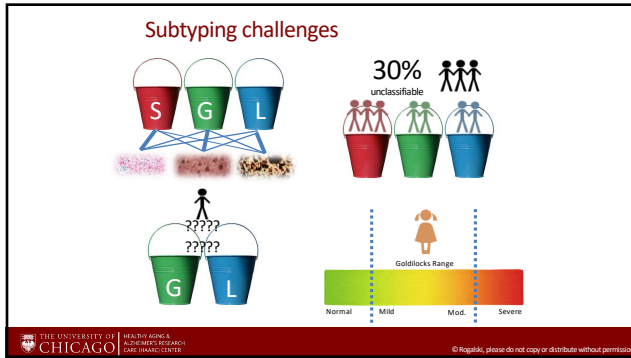
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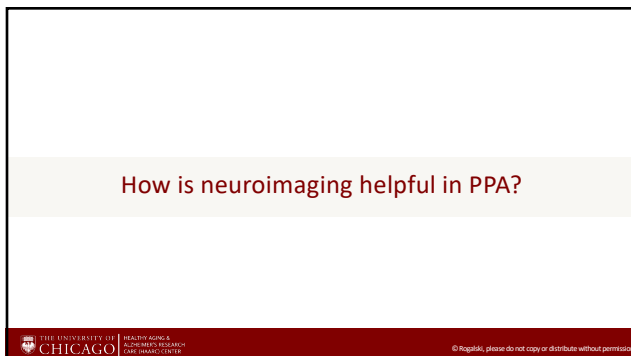
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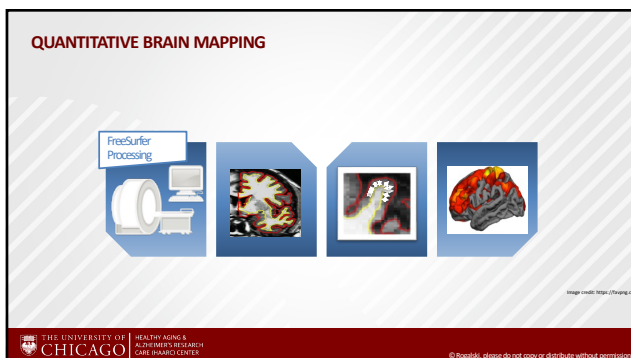
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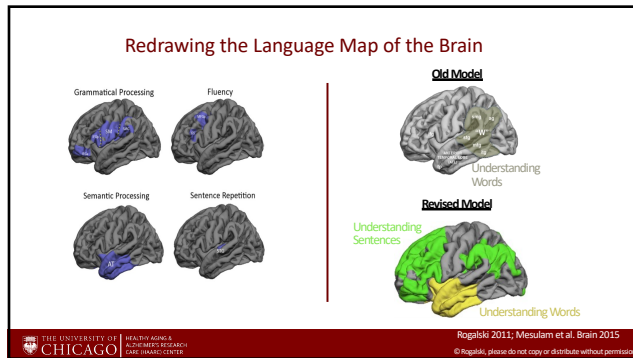
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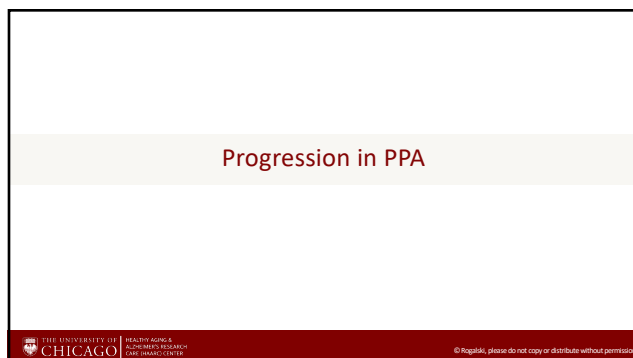
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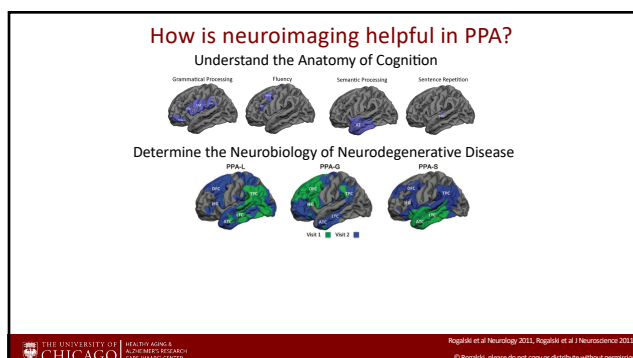
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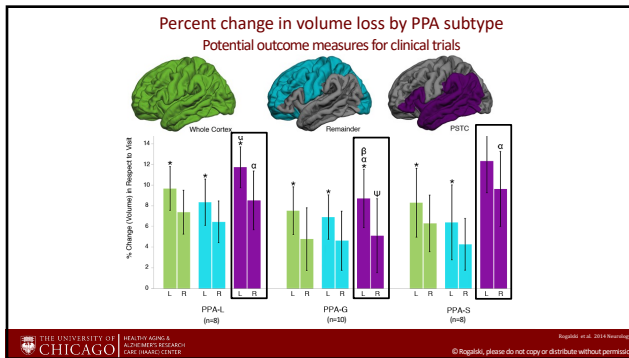
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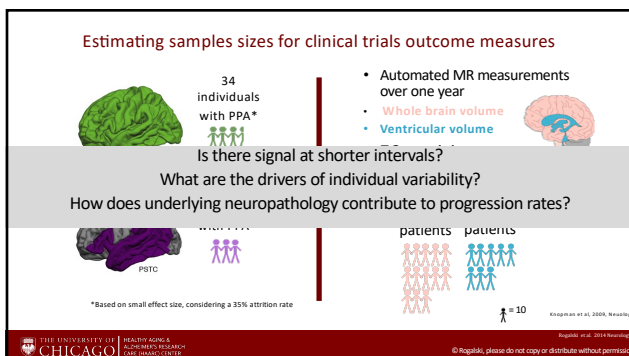
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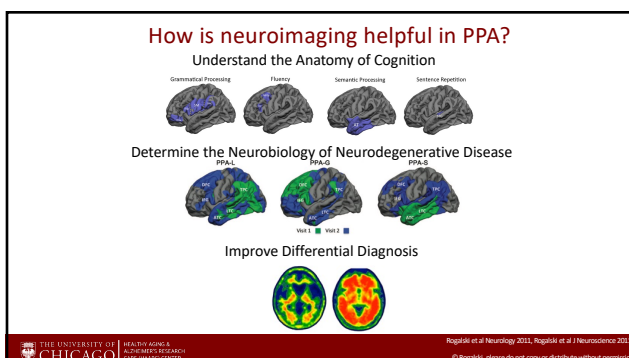
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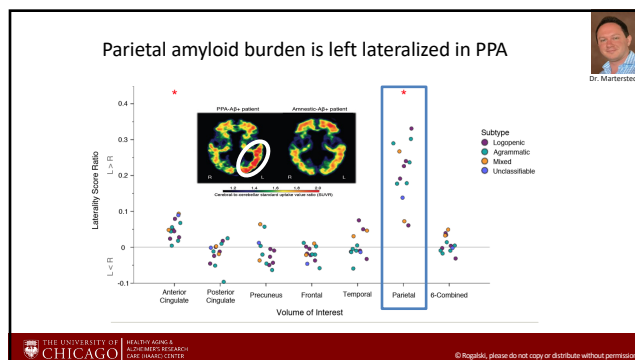
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**Progression at clinically relevant intervals in the aphasic variant of AD**

	PPA <sup>AD</sup>	PPA <sup>AD</sup>
N	17	9
Age at initial visit	66.3 (5.8) [58-80]	70.8 (7.2) [61-82]
Gender (% M)	8 (47%)	5 (56%)
Education	16.4 (2.4) [12-20]	15.0 (2.2) [12-19]
Initial visit symptom duration	5.2 (2.8) [1.4-10.9]	3.9 (1.3) [2.1-6.0]
Months between visits	6.3 (0.5) [5.5-7.6]	6.1 (0.3) [5.2-6.7]
Subtype		
Logopenic	10 (59%)	2 (22%)
Aggramatic	7 (41%)	7 (78%)

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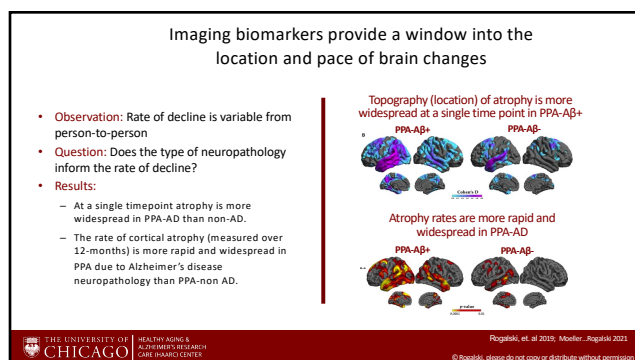
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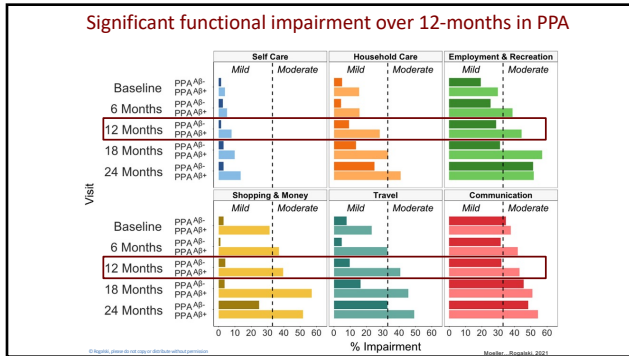
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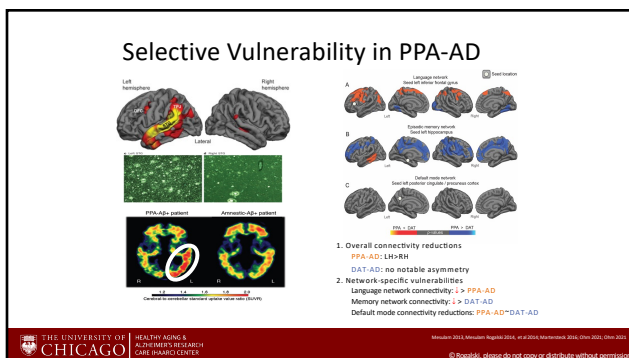
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**Aphasic-AD & Amnesic-AD:**  
Heterogeneity & Selective Vulnerability of Alzheimer's disease neuropathologic change

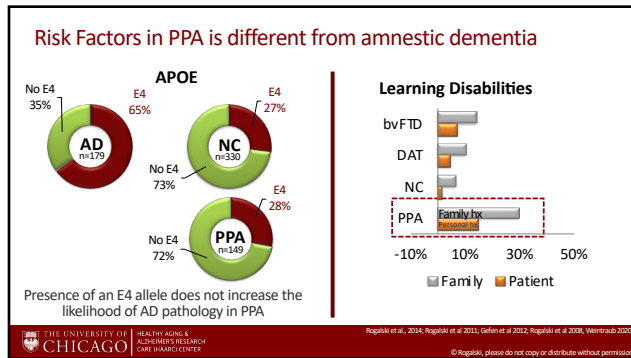
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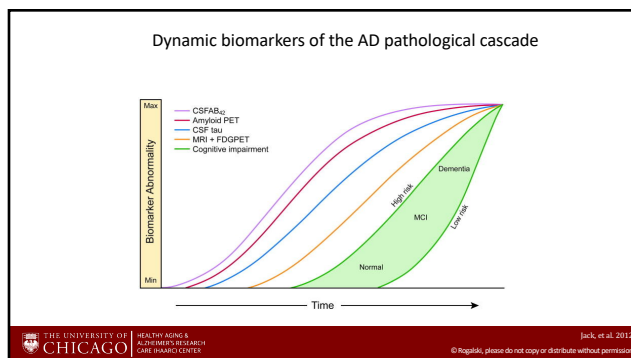
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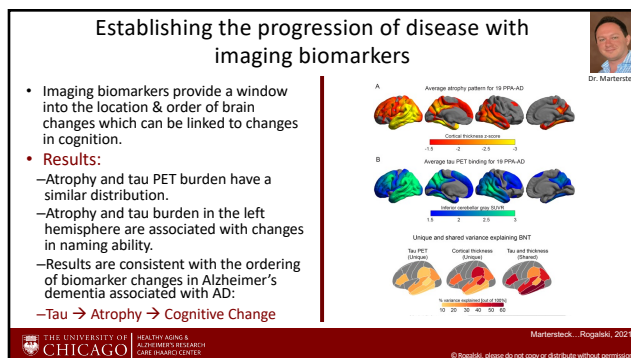
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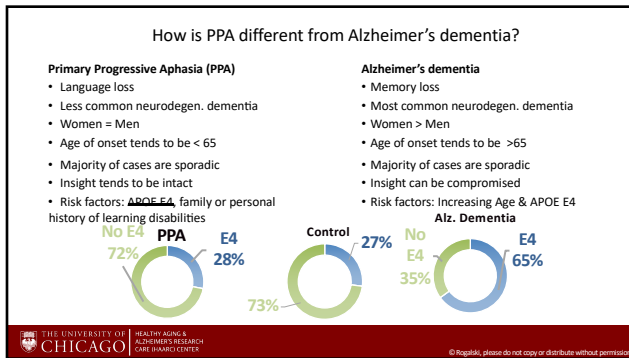
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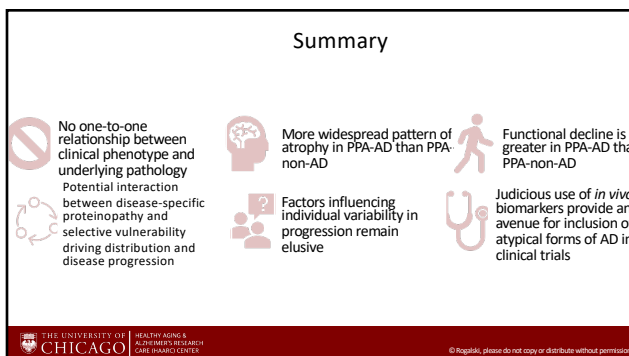
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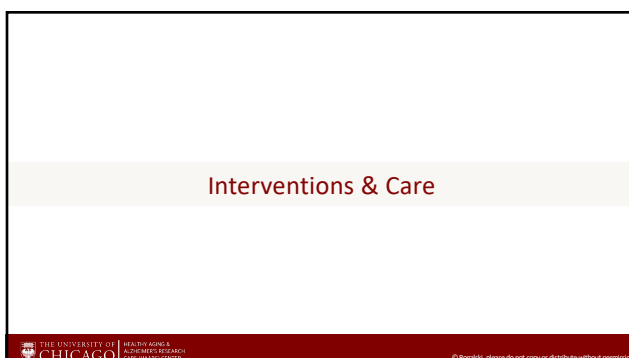
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### Who can provide care? Building a Care Team

Communication is critical among the interdisciplinary team members

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### Interventions, Care, & Support

#### Pharmacologic Treatments

- Currently, there are no definitive options to halt or reverse the neurodegeneration, but this is an active area of research
- Limited options to target symptoms (e.g., depression, anxiety, trouble with sleep, etc.)
- Disease modifying treatments targeting Alzheimer's disease neuropathology may be appropriate for those with AD biomarkers (e.g., Cholinergic trials, AD immunotherapies including lecanemab, donanemab)
- Veri-T trial (Verdiperstat for svPPA): Phase I RCT
- FTLD-Tau Trials: Anti-tau monoclonal antibody trials, small molecules for tauopathies (sodium selenate)
- Gene therapy trials: FTD due to progranulin mutations

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### Historic (and sometimes current) Barriers to Care for PPA

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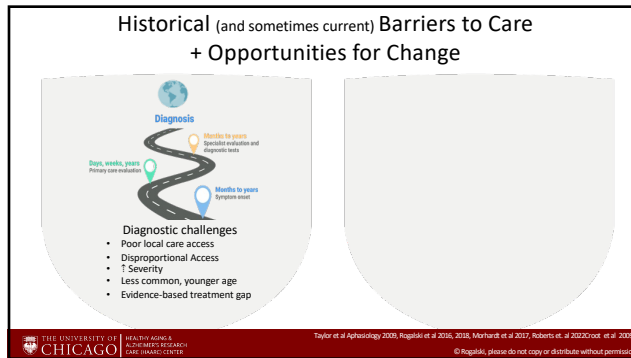
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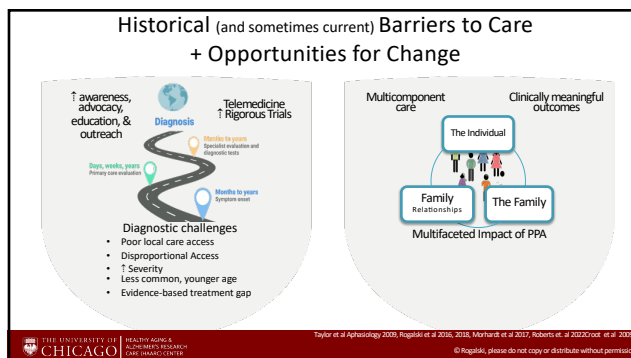
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### Interventions, Care, & Support

- Non-pharmacological interventions
  - Art therapy
  - Music therapy
  - TdCS/TMS
  - Caregiver Interventions
  - Multidisciplinary Interventions
  - Support Groups
  - Speech-language therapy\*

Artwork by R.S. after 2 years of living with a diagnosis of PPA. (from Mesulam et al. 2014)

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### Support Group Models for PPA

Traditional | Educational | Activity | Online



- \* Coping with limitations & language decline
- \* Sense of belonging
- \* Confronting Stigma
- \* Expressing Resilience

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### Speech language therapy

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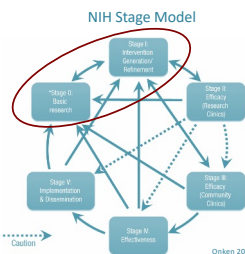
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### Progress, Momentum, & Balanced Optimism

Systematic review: non-pharm interventions for PPA/PPAOS

- Early PPA Interventions = Encouraging
- Few high-quality studies
- No Randomized Controlled Trials



NIH Stage Model

Onken 2014

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Bridging the Gap & Elevating the Science: Addressing Unmet Needs

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**communication BRIDGE™**  
 Maximizing communication participation and quality of life for persons with PPA and their communication partner(s)

Client-directed with consideration of real-world needs

Dyadic

Improving access to care through telemedicine

Custom web-application

Iterative, collaborative, & dynamic assessments to guide goal setting, multicomponent interventions, and communication participation

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Kagan, Aphasiology 2008; Rogalski et al. 2018; Rogalski et al. 2018; Roberts et al. 2022

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Tailoring Technology:  
 Settings, skills, needs, & interests



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**Tailoring technology in Communication Bridge**  
Settings, skills, needs, & interests



Improving Access to Expert Care through Telemedicine




Resources, Intervention, Exercises, Education, Motivation



Extension of Participation in Meaningful Activities

Technology is implemented in a way that is relevant to the dyad and maximizes the rigor, reliability, and reproducibility of the intervention



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**communication BRIDGE web application**

communication BRIDGE

Sign In

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**communication BRIDGE web application**

communication BRIDGE

H. Demo

[HOME](#)
[RESOURCES](#)
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SIGN OUT

**To do list**

This week's tasks

**WEB EXERCISES**


- Picture Cards
- Pronunciation Cards
- Word to Picture Matching
- Script Practice

**VIDEOS**

- PPR Overview
- Introduction to Communication Bridge Web-A...

Welcome to Communication Bridge

Click on the To do list items to get started



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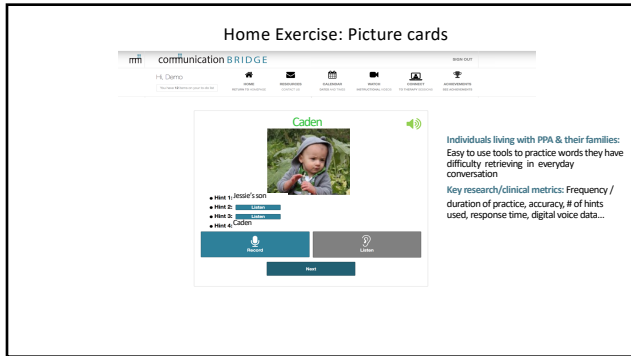
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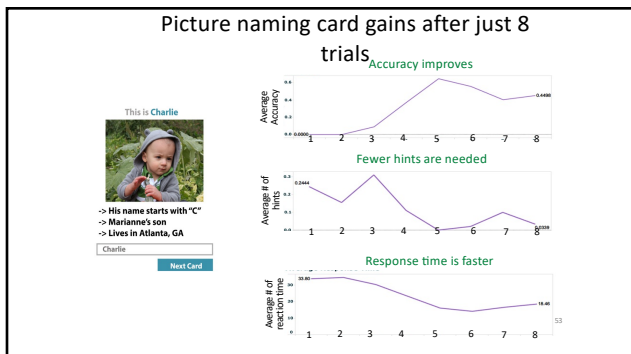
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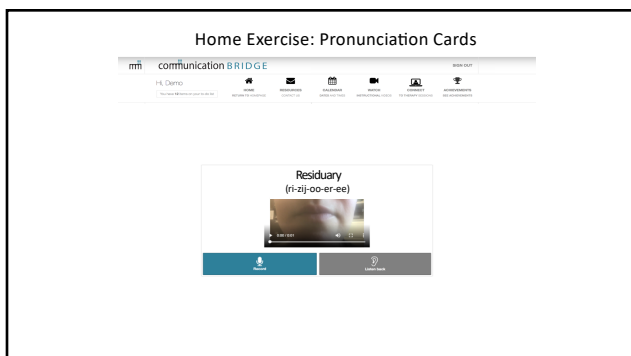
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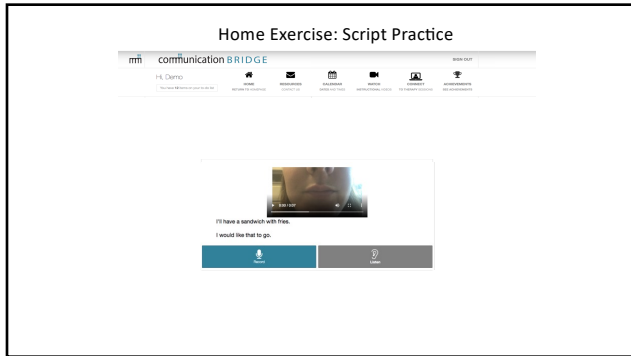
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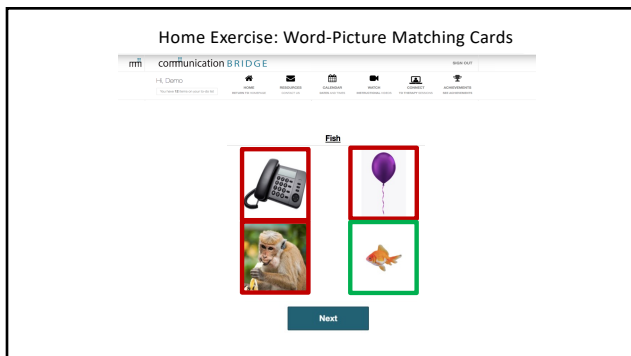
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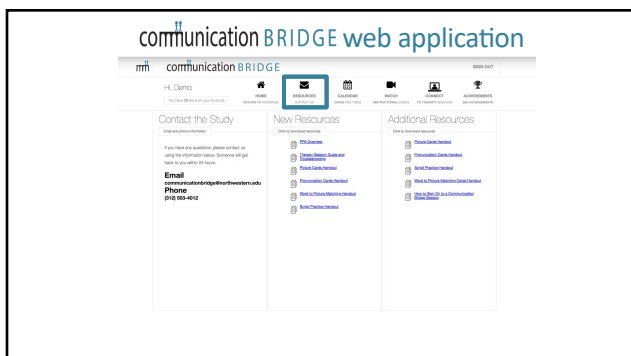
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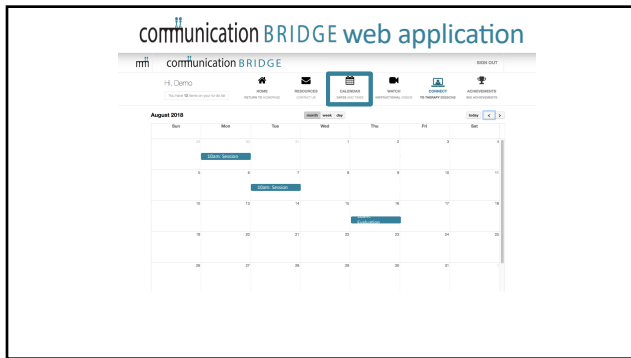
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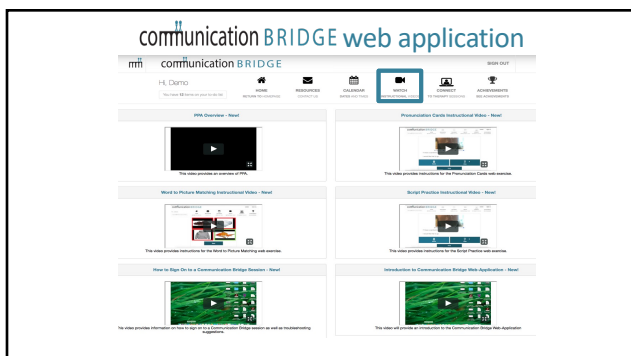
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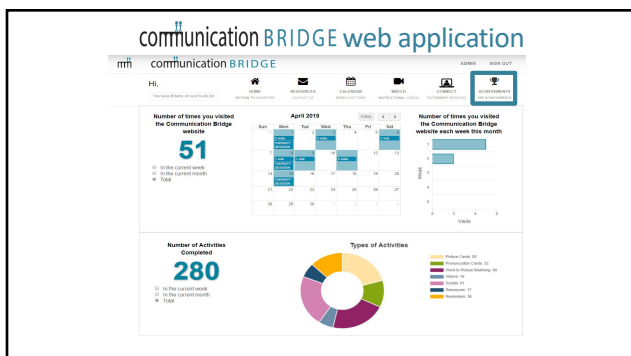
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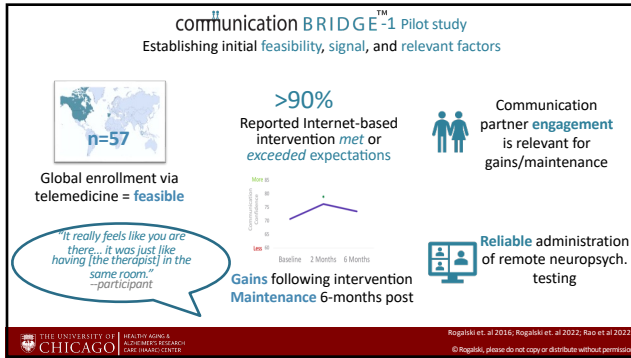
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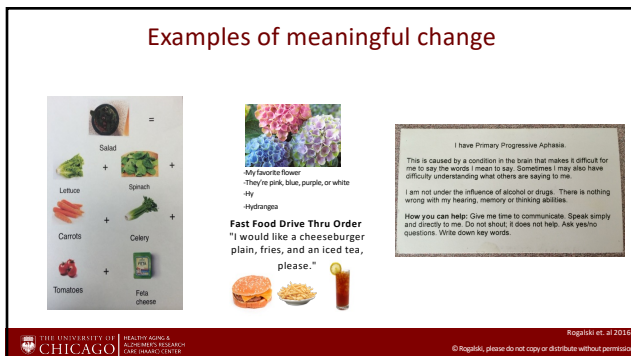
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**Script Example**

**Explaining my PPA**

"I am losing my words.

It is a relatively rare neurological condition called PPA, Primary Progressive Aphasia.

My speech has slowed down.

I have to plan out each word, one syllable at a time. PPA only affects my speech, nothing else.

It does not affect my mind and intellect.

My good friends say that an attorney without words is a real blessing! So, bear with me."

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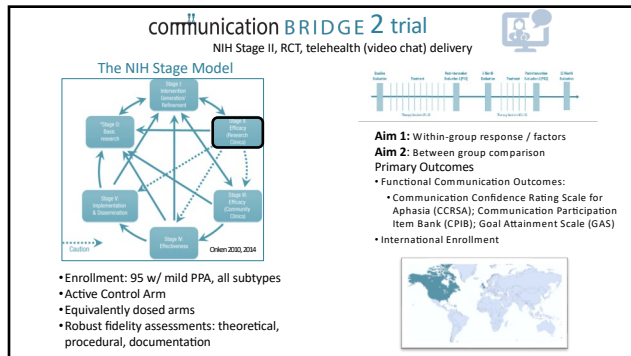
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**communication BRIDGE 2 trial**  
Optimizing Rigor: NIH Stage II, RCT, telehealth (video chat) delivery

Baseline Block 1 Post 82 8.2 12mo

Trials work:

**Key Take Home Points:**

- Trial design meets the rigor required for pharmacologic trials
- Includes clinically meaningful outcomes
- With mild to moderate primary progressive aphasia
- Participant-reported comes: allows for

Blinded Participant

Angela C. Roberts<sup>1</sup>, Alfred W. Rademaker<sup>2</sup>, Elizabeth Ann Salley<sup>3</sup>, Aimee Mooney<sup>4</sup>, Dorthy Mohrhardt<sup>1</sup>, Melanie Fried-Oken<sup>5</sup>, Sandra Weintraub<sup>6</sup>, Marel Mesulam<sup>7</sup> and Emily Rogalski<sup>8</sup>

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Rogalski et al. 2024, 2025; Roberts et al. 2022  
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Iterative, Collaborative, & Dynamic Assessment to guide goal setting, interventions, and communication

- Independence:** What can the individual still (or potentially) do independently?
- Personal identity:** What provides purpose and motivation?
- Knowledge & Insight:** What is their understanding of the disease, its progression, and their strengths/limitations?
- Viewpoints:** Consideration of input from multiple stakeholders (person with PPA, friends, family, clinicians, etc.)
- Expectations:** What are their expectations?
- Environmental supports:** What are the communication environments?

Personalized communication strategies

Communication partner training

Environmental modifications

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### Demographics & Clinical Characteristics

Characteristics	Total N
Self-reported Sex	Male : Female
	49:46
Self-reported Ethnicity	Hispanic / Latino
	1
	Not Hispanic / Latino
	94
	Unknown / Not reported
	0
Self-reported Race	White
	94
	Asian
	1
PPA Subtype	PPA-L
	43
	PPA-G
	26
	PPA-S
	26
Sx Duration @ Baseline	Mean of baseline duration
	3.7 ± 1.8
	Range
	0.4 – 9.6
Communication Partner Relationship	Spouse (long-term partner)
	84
	Relative (parent, sibling, etc.)
	5
	Other (friend, neighbor)
	6
PPA Pt Age at Baseline	Mean of baseline duration
	67.1 ± 7.2
	Range
	52-82

Recruitment takes a village. Thank you for the referrals!

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### Key Statistical Analysis Features

- Randomized groups compared on 3 primary outcome measures:
  - Communication Confidence Rating Scale (CCRSA)
  - Communicative Participation Item Bank (CPIB)
  - Goal Attainment Scaling (GAS)
- Intent-to-treat principle followed
- Marginal linear model, considering repeated measures
  - Model includes all visits, no adjustment for baseline
- Overall two-sided alpha level of 0.05

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### CCRSA

Communication Confidence Rating Scale for Aphasia

CCRSA is a 10-item patient-reported outcome metric (PRO)

0 10 20 30 40 50 60 70 80 90 100

Not Confident Moderately Confident Very Confident

Example CCRSA Questions

- How confident do you feel about your ability to talk with people?
- How confident do you feel about your ability to stay in touch with family and friends?
- How confident do you feel about your ability to follow news and sports on TV?
- How confident do you feel about your ability to speak on the telephone?
- How confident do you feel that people include you in conversations?

- Superiority analysis threshold: Not met
- Experimental group
  - Non-significant increase after each intervention block
  - Response shape is consistent with what we would expect in a responsive intervention
- Control group
  - Non-significant increase after intervention Block 1, followed by steady decline

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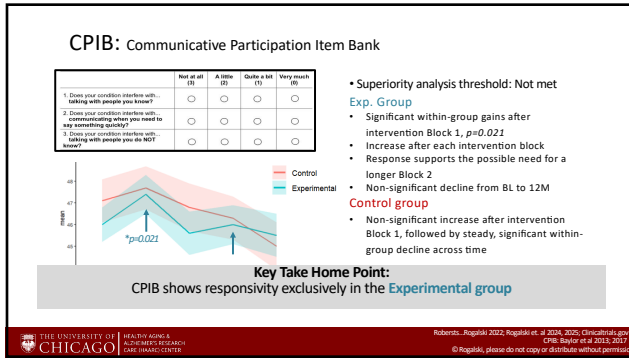
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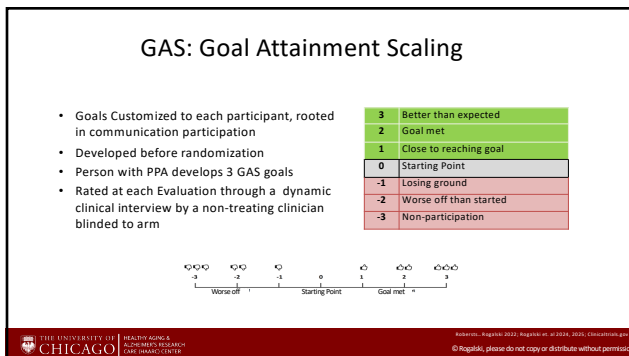
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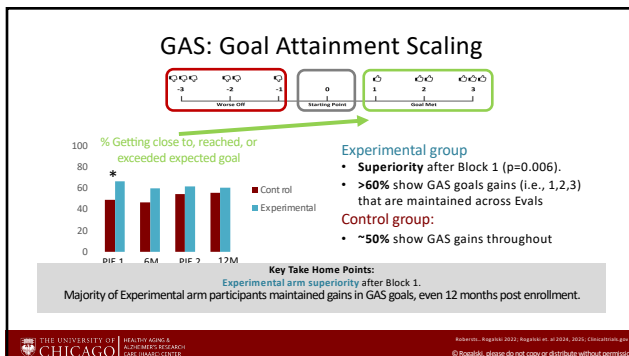
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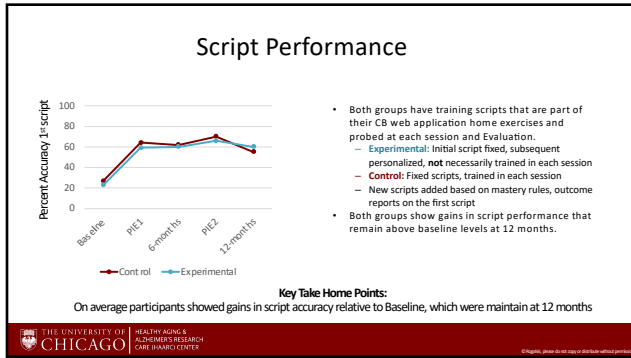
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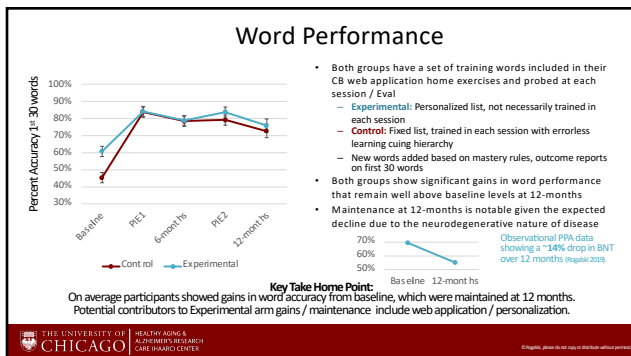
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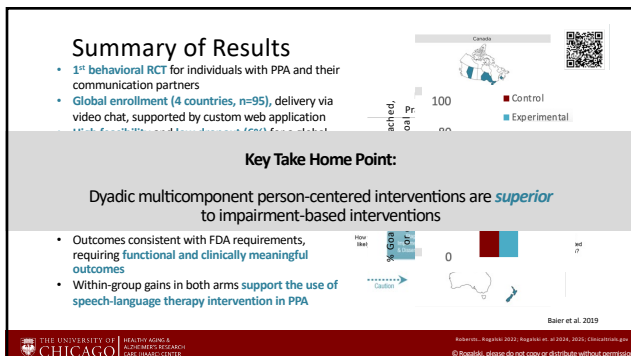
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**An Example of Meaningful Change:**  
Maximizing Access to language, communication, & life participation

Naming Personally Relevant Pictures  
Pre-Intervention

communication BRIDGE

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**Summary**




There is no one-size-fits all way to describe the spectrum of changes in PPA (or other neurodegenerative dementias)




Use of technology can be tailored to the needs, experience, and interests of the individual



Technology can support person-centered, life participation approaches with a goal to maximize quality of life for those with PPA



Reliable assessment of language function is possible using video chat technology



Telemedicine provides an opportunity to improve access to care for those living with PPA

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References: Repaski 2022, Repaski et al 2024, 2025, cdc.com/aging  
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Path to Implementation

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## Beginning with the end in mind

### communication BRIDGE™ 3 Trial

Phase 2b, NIH Stage II, RCT, telehealth (video chat) delivery

**Efficacy of integrated multi-clinician care:**  
Dyadic, multi-clinician intervention (speech language therapist + social work), framed in participation-based models of care

- Speech language intervention + psychosocial education and counseling

**Planning for Implementation:**  
Readiness Assessment for Pragmatic Trials (RAPT); Cost Analysis

**Wearable Sensors:**  
Capture objective dimensions of life participation

**Stakeholder Engagement:**  
Interprofessional Implementation Advisory Board, Family Advisory Board

Readiness Assessment for Pragmatic Trials (RAPT)

Baier et al 2019

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## communication BRIDGE™ 3 trial

### web application

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## Connecting to support

The Association for Frontotemporal Degeneration  
Dementia care experts

Deutsche Alzheimer Gesellschaft e.V.  
Selbsthilfe Dementie

Alzheimer's Research UK  
Make breakthrough possible

Life's a Conversation  
Dementia care experts

alzheimer's wa  
the dementia care experts

Rare Dementia Support  
Join a community learning

dementia australia  
Dementia care experts

Aphasia Association  
Dementia care experts

FRANCE dlt  
Dementia care experts

https://www.theaftd.org/get-involved/in-your-state/canada/  
https://www.theaftd.org/get-involved/in-your-state/international/  
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**CR2 Contributors & Collaborators**  
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 Melanie Fried-Chen | Alayne Mooney  
 Darby Morhardt | Sara Shauhanfield  
 Marissa Esparza | Matt Bona  
 Zoe Steeney | Krista Kach  
 Libby Rogers | Jecly Khayum  
 Marisel Mesulam | Sandra Weintraub  
 Leslie Rao | Erin Blase | Ollie Fegter

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 Eric Polley | Ollie Fegter  
 Emily Cummings | Sydney Branson  
 Allison Chen | Thomas Hopkins  
 Emily Kaderabek | Roshnee Burma  
 Alexis Robinson-Osler | Lauren Lightbody  
 Ben Heller | Rhiana Schaffer  
 Phyllis Timpo

### With Gratitude

Special thanks to our participants for their time & commitment to research, without them none of this work would be possible.

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R01AG055425	P30AG13854
R01NS075075	U54NS092089
R01	
R01DC008552	

**Now Enrolling!**  
**communication BRIDGE-3**

**Trial Location:** All study components take place remotely via video chat (Zoom)

**Trial Length:** ~18 months

**Trial Activities:** Participants will receive intervention sessions with licensed clinicians

**Trial Costs:** There are no costs to participate. Compensation will be provided.

**If interested, contact the study team for more info:**

[CBtrial@uchicago.edu](mailto:CBtrial@uchicago.edu)  
[hsarc.center.uchicago.edu/communication-bridge](https://hsarc.center.uchicago.edu/communication-bridge)  
 1-855-824-7887

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