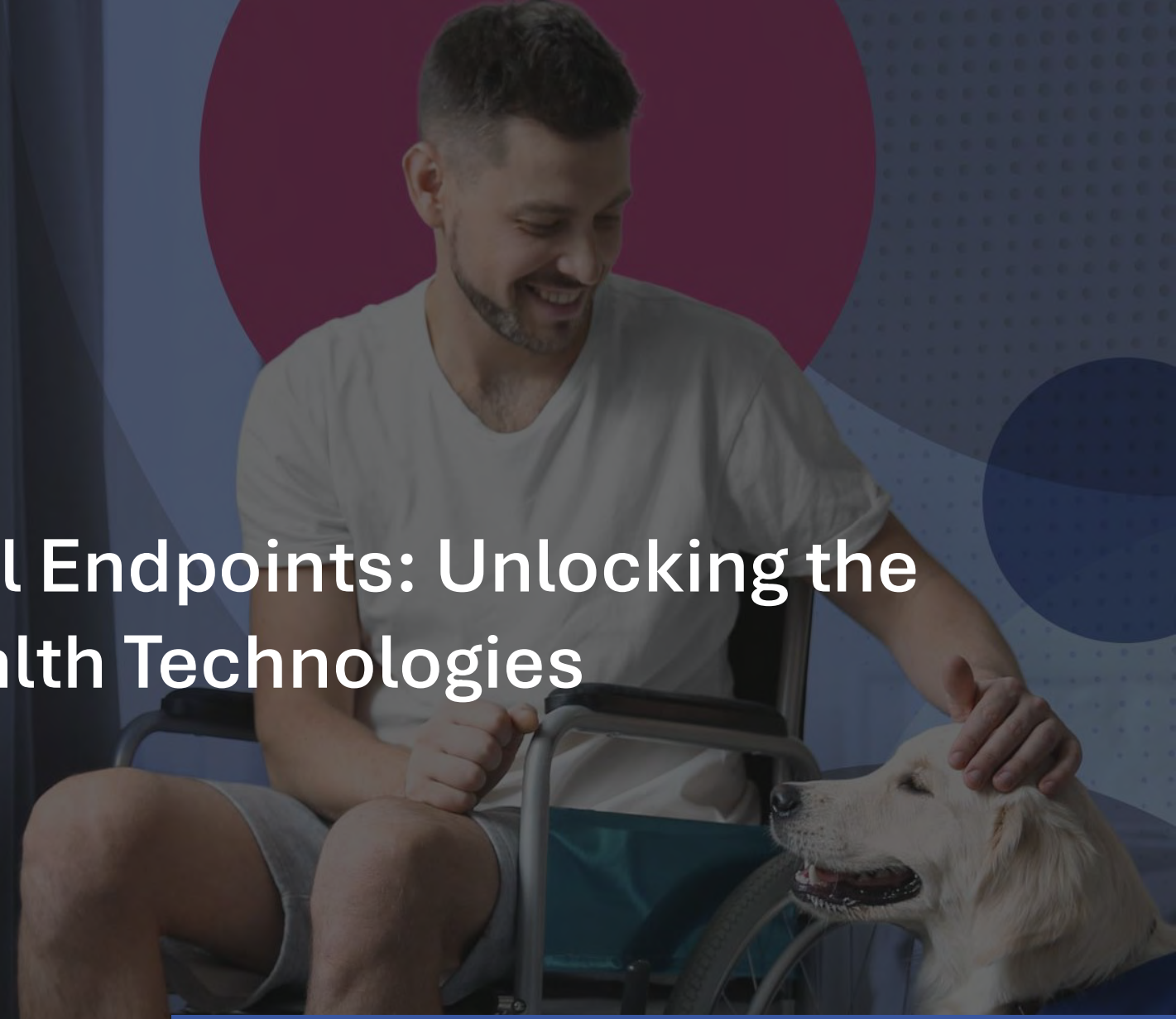
Ametris

Digital Health Monthly Webinar

# Redefining ALS Clinical Endpoints: Unlocking the Potential of Digital Health Technologies

October 14, 2025



**NEXT MONTH Digital Health Monthly topic:**

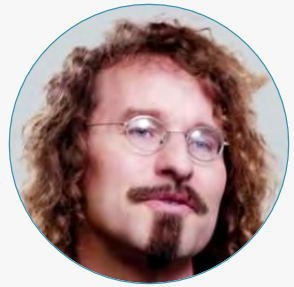
ADDS 2025 Reflections: Key Learnings from Basel and a Preview of the 2026 Annual Meeting

# Agenda

- Introductions
- North Star ALS: *Why DHTs matter to ALS patients/caregivers*
- Ametris: *ADDS 2025 ALS workshop findings*
- Modality.AI: *Self-Guided ALS Assessments*
- ZEPHYRx: *Remote respiratory monitoring*
- Panel Discussion
- Q&A

Dr. Nadia Sethi
Founder, Patient Advocate
*North Star ALS*

Adam LaPrad, PhD
Head of Product and Scientific Affairs
*ZEPHYRx*



David Suendermann-Oeft
Chief Executive Officer
*Modality.AI*

Collin Hovinga
PharmD, M.S., FCCP, Vice President of Rare and Orphan Diseases
*Critical Path Institute*

Rakesh Pilkar, PhD
Lead of DHT Solutions, Neuroscience
*Ametris (formerly ActiGraph)*

? Ask your questions in the chat

# Why Digital Health Technologies Matter to People Living with ALS & Caregivers

**Nadia Sethi, DDS**

North Star ALS

# The Challenges of ALS

- ALS has strong unmet needs
- Trial failures may occur because measures are not objective, sensitive, and continuous
- Families face high disease burden including exhausting and expensive travel for care and research
- Measures should reflect the flow of our daily lives, not a snapshot at a clinic visit

# Why Digital Health Tech Matters to ALS Families

Familiar, accessible technologies can **make research more inclusive**

Continuous, objective, and sensitive measures **from home**

**Reduced travel and financial burden and fatigue**

Empower people living with ALS to **contribute meaningful data**

# 2025 Actigraphy Survey: 76 U.S. Adults Living with ALS

- **97%** felt actigraphy would be valuable for tracking progression
- **100%** were willing to wear a device and **80%** would wear 2+ devices
- **76%** would wear devices all day
- Top concern: Comfort (48%); **35% had no concerns at all**
- **64%** felt it would reduce travel burden

- **Over 90%** believed actigraphy could track walking/gait and hand and arm movements
- **85%** felt it could track sleep

# What This Means for the ALS Community

- People living with ALS are ready for digital measures
- Digital measures could reduce burden, increase access to care and research, and improve data quality
- Collaboration between patients, researchers, and regulators is essential
- DHTs may capture data that are more reflective of our daily lives

Ametris

# ADDS 2025 ALS Workshop

*Findings & key takeaways*

Digital Health Monthly | Ametris

ADDS 2025
ACTIGRAPH DIGITAL DATA SUMMIT 2025
FEBRUARY 10-12 | PENSACOLA BEACH, FL

# ALS drug development

## The current need

- There is an urgent need for more sensitive, patient-centric and objective measures of disease progression and treatment effect.
- Sensitive measures in early-stage trials can provide early evidence of treatment effect, encouraging investment for further development.

- **The ActiGraph Digital Data Summit (ADDS) 2025 ALS workshop** brought together experts from academia, industry, regulatory agencies, and patient advocacy groups.

- **Objective** - To explore how digital health technologies (DHTs), specifically actigraphy-based measures can help accelerate ALS drug development and approval.

# ADDS 2025 ALS Workshop

## Recap

### Participants

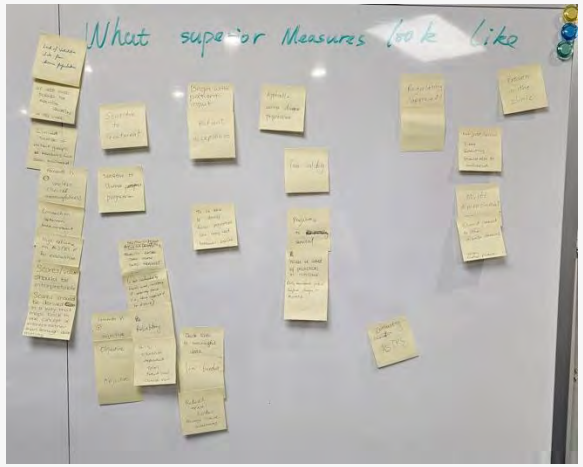
pwALS, caregivers, academic researchers, clinicians, biostatisticians, industry scientists, DHT developers, clinical operations leads, regulatory experts, and representatives from patient advocacy groups

### Agenda

- Current Measurement Tools and Clinical Trial Use Cases,
- Novel Digital Tools and Industry Adoption
- Evidence Generation and Regulatory Readiness.

### Activities

Presentations, white-board activities, round-table discussions




ADDS 2025
ACTIGRAPH DIGITAL DATA SUMMIT 2025
FEBRUARY 10-12 | PENSACOLA BEACH, FL

# ADDS 2025 ALS Workshop

## Key takeaways

# ADDS 2025 ALS Workshop

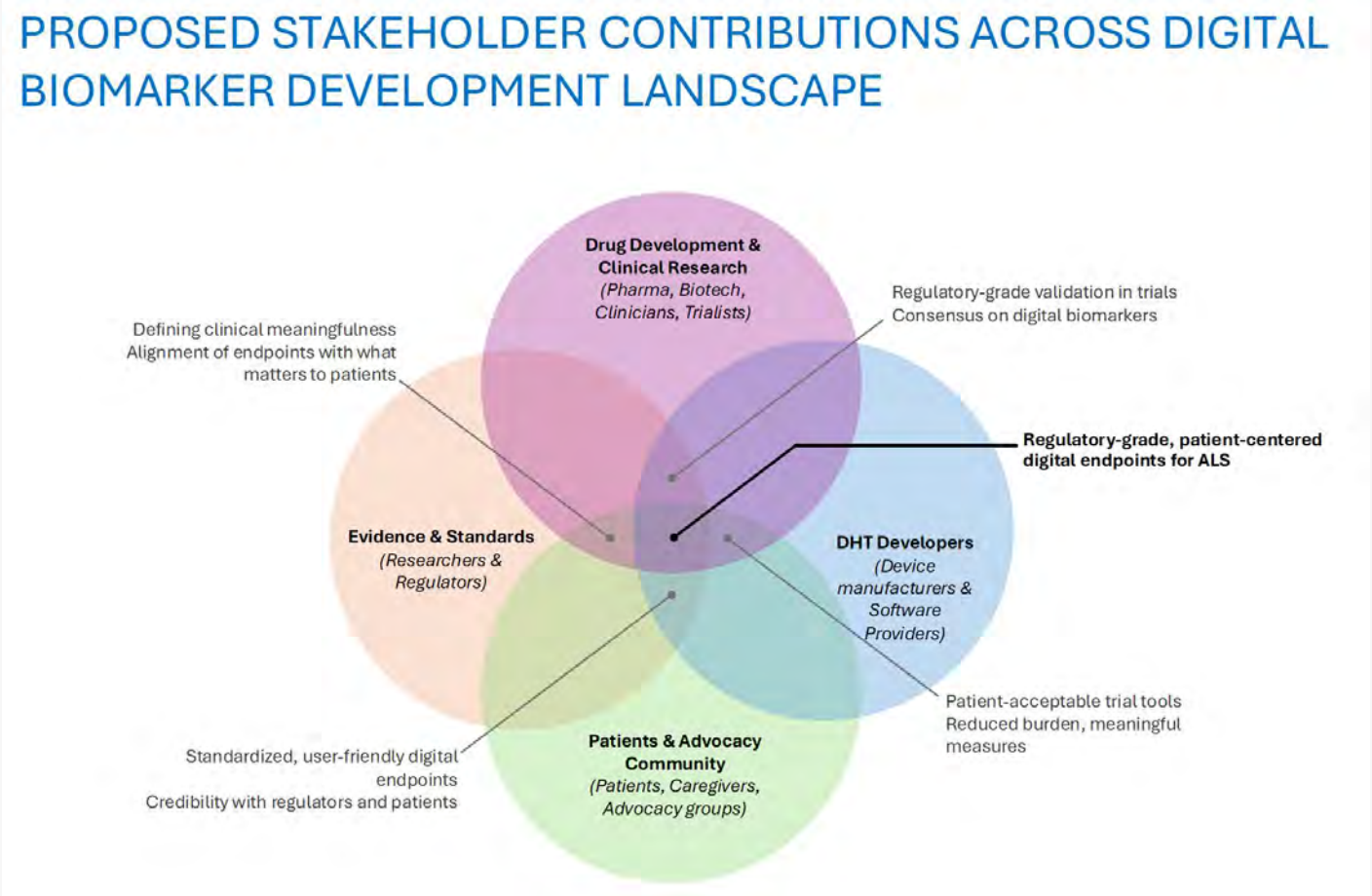
## Key takeaways

Evidence generation requirements for sponsor buy-ins and regulatory acceptance

| Evidence Needed | Sponsors' buy-in | Regulatory acceptance as surrogate biomarkers or intermediate clinical endpoint (Accelerated approval) | Regulatory acceptance as a primary or secondary endpoint (Full approval) | Priority |
|---|---|---|---|---|
| Improved sensitivity over the ALSFRS-R | X | | X | High |
| Strong measurement properties (low variability, high reliability) | X | X | X | High |
| Correlations with clinical scales (construct validity) | X | X | X | High |
| Ability to detect treatment effect | X | X | X | High |
| Precedence of success in other studies | X | | | Moderate |
| Prioritizing a measure or two over many | X | | | Moderate |
| Encouragement from regulatory bodies | X | | | Moderate |
| Explicitly defined measure | | | X | Moderate |
| Prognostic value | | X | | Low |

# ADDS 2025 ALS Workshop

## Key takeaways




ZEPHYRx

# Refining ALS Endpoints with Remote Respiratory Monitoring

Adam LaPrad, PhD
Head of Product & Scientific Affairs, ZEPHYRx

# Agenda

1. About ZEPHYRx
2. Challenges in ALS Trials
3. Our Decentralized Solutions
4. Case Studies
5. Looking Forward

# About ZEPHYRx

**2019**

**Founded with a focus on Specialized Respiratory Solutions**

**2020**

**COVID-19: Partnered with Cystic Fibrosis Foundation to monitor every CF patient in the country**

**Today**

**Industry-leading cloud platform for respiratory care**


**>30** countries served

**>1.4M** pulmonary function tests

**>1k** trial sites supported

**650** hospital MSAs

# **Challenge:** Lung Function is an Important but Burdensome Endpoint in ALS Clinical Trials

ZEPHYRx

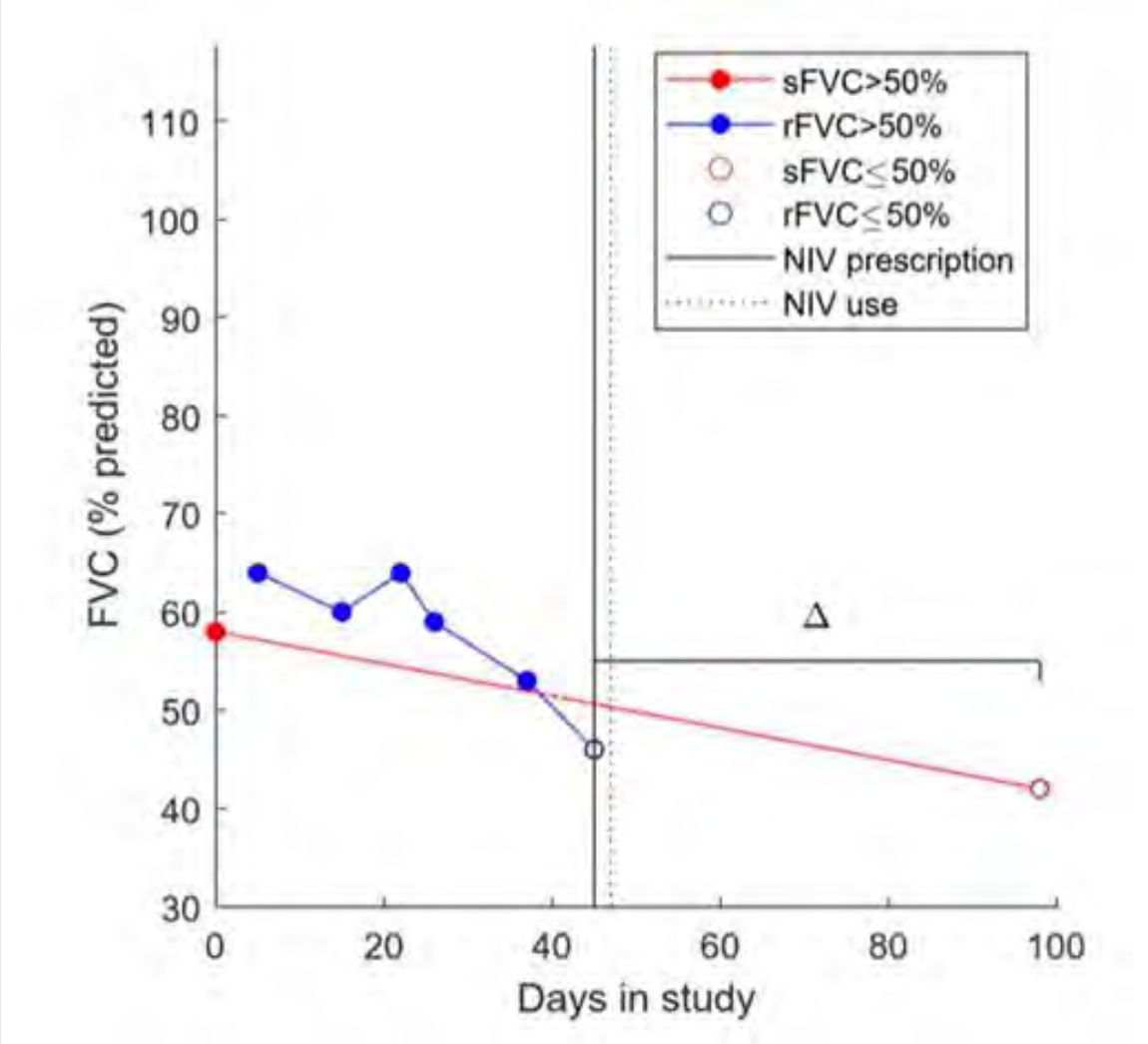
**Why spirometry matters:**

- Measures how much air a person can exhale – a direct window into respiratory muscle strength
- Links ALSFRS-R changes to measurable respiratory function changes
- Quantitative, FDA-recognized physiologic endpoint

**27%** of ALS clinical trial patients withdraw from clinical trials due to travel difficulties and caregiver burden

Kiernan et el., Nature Reviews Neurology, 2021

# **Challenge:** Changes in Lung Function may be Missed between In-Clinic Visits




Gerônimo & Simmons, Journal of the Neurological Sciences, 2024

Weekly remote spirometry (rFVC) resulted in a ~2-month advance notice of NIV need*, compared to quarterly site visits (sFVC)

*NIV need defined as a drop in FVC below 50% predicted

# Our Decentralized Respiratory Solutions

ZEPHYRX Kiosk™



ZEPHYRX Home™


**ON-SITE**

- Spirometry
- Disease-specific additional endpoints
- eCOA

**AT-HOME**

- Spirometry
- Disease-specific additional endpoints
- ePRO

***Automated data delivery – no manual data entry.***

# ZEPHYRx Home: Patient Experience

**FDA-Cleared Spirometer**


**Breathe Easy Mobile App**


**Patient Onboarding:**

1. Unbox spirometer
2. Scan QR code to download ZEPHYRx Breathe Easy app
3. Connect spirometer to app via Bluetooth
4. Follow on-screen instructions

**> 50,000 delivered to patients' homes**

# ZEPHYRx Home: Remote Respiratory Visits

**Workflow:**

1. In-app video call initiated by a registered respiratory therapist (RT) specialized in ALS
2. RT coaches patients through spirometry maneuvers
3. RT ensures quality control via real-time data streaming

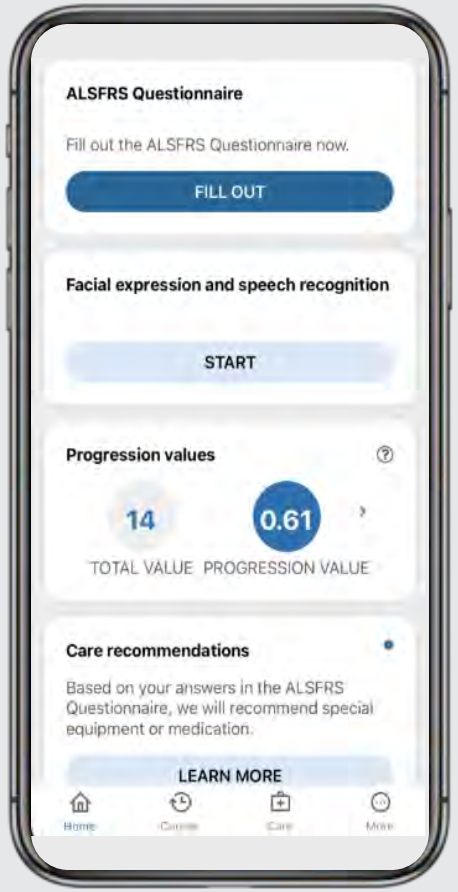
**Digital Endpoints:**

- Forced spirometry (e.g., FVC, FEV1)
- Slow spirometry (e.g., SVC)
  - Seated and Supine

**86%**
**compliance**

**300+ patient global ALS decentralized trial**

# ZEPHYRx Home: Self-Reported Endpoints

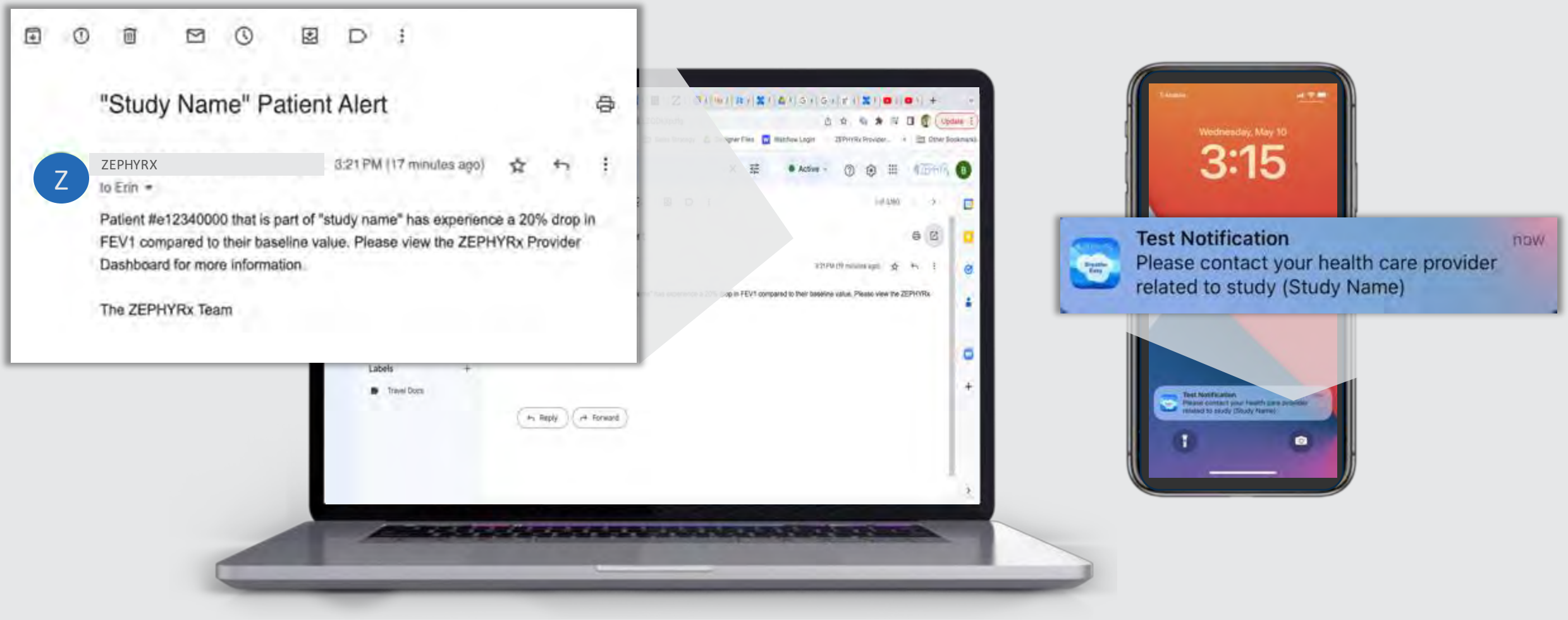

## Digital Endpoints:

- Spirometry
- Daily Symptom Diary
- ALSFRS-R

## 89% Compliance

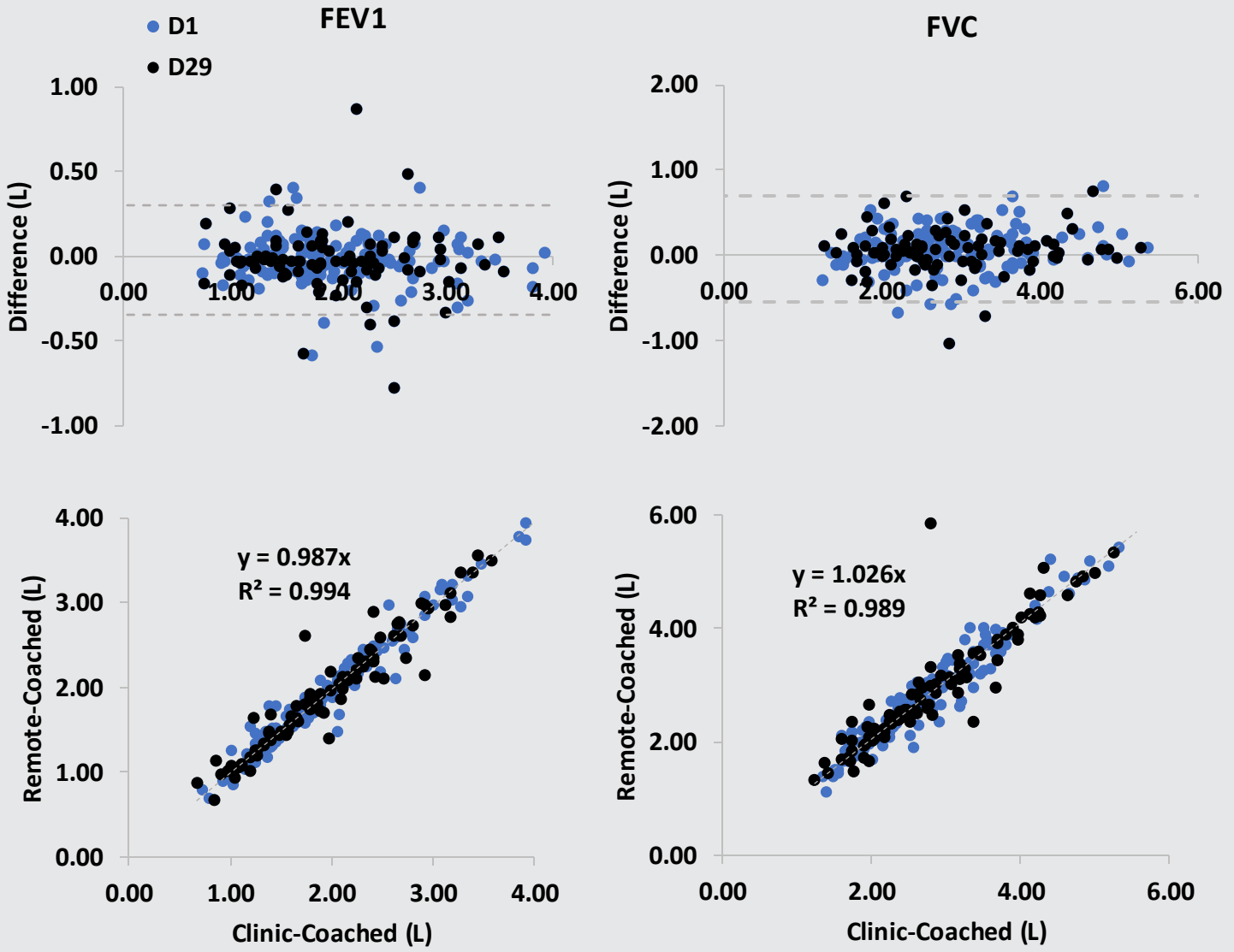
400 participants conducting independent spirometry and symptom diaries twice per day

# ZEPHYRx Provider Dashboard: Patient Safety Alerts



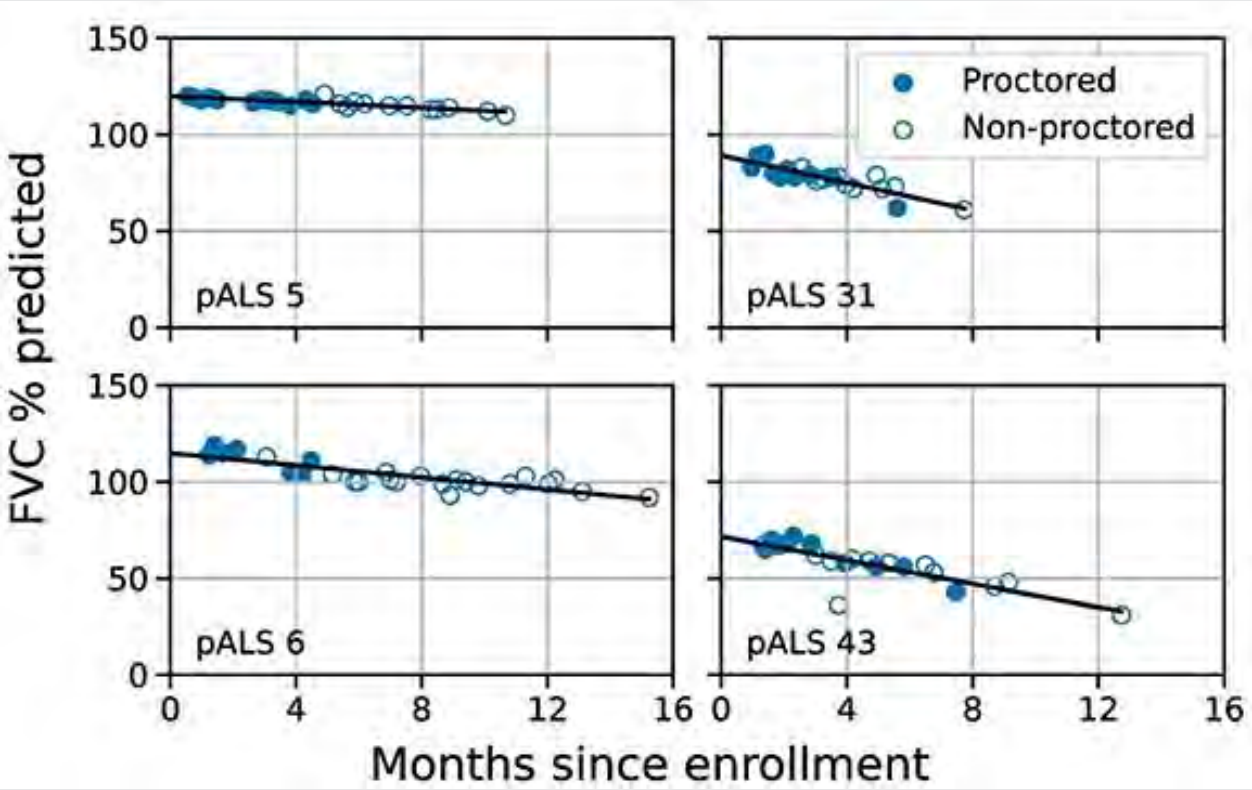
# **Case Study:** Remote coached spirometry has high concordance with in-clinic coached spirometry

- Global Phase II Clinical Trial
- 406 paired tests
- FEV1: -0.02 ± 0.17L
- FVC: 0.08 ± 0.32L




Dosanjh et al, ERS, 2025

# Case Study: Validation of Decentralized Respiratory Endpoints for ALS Studies



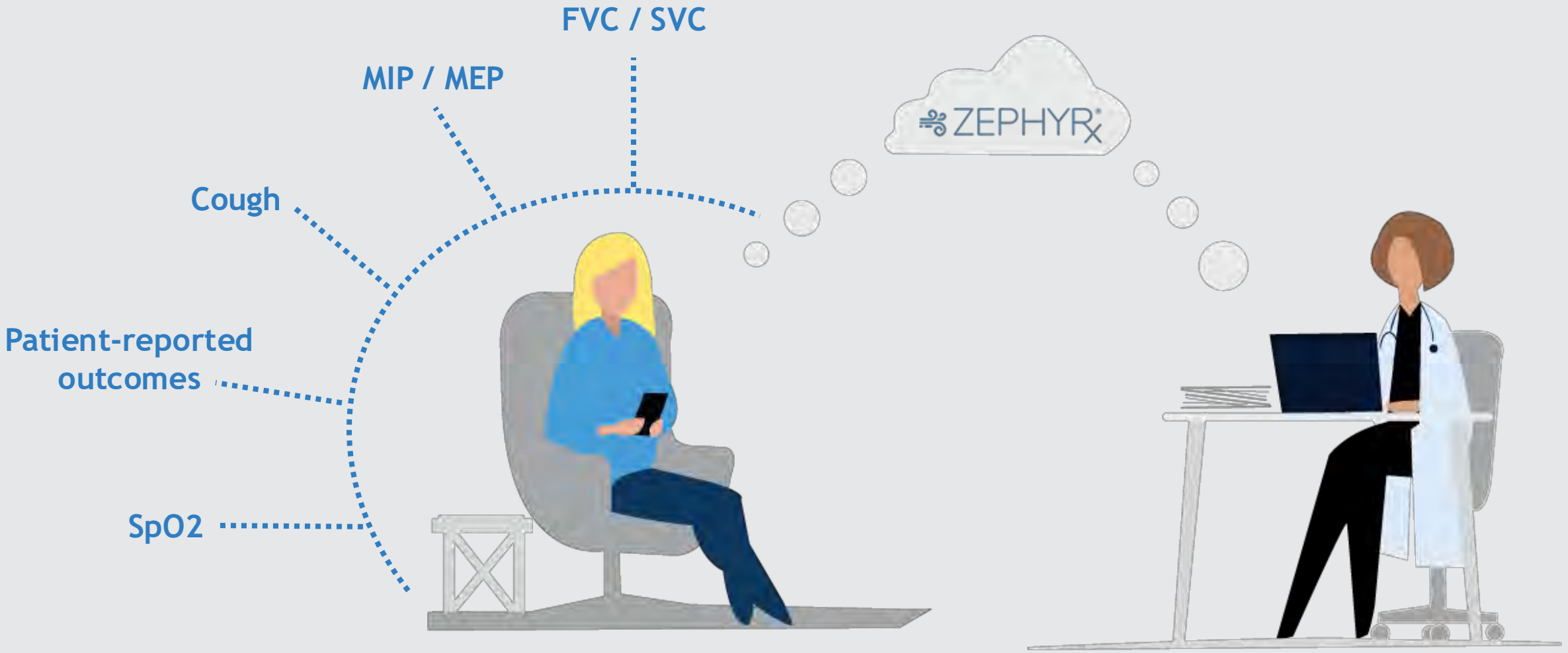

- 991 FVC and 929 SVC sessions
- Data quality and slopes were statistically identical between proctored and non-proctored ($t = -0.4$, $p > 0.69$)
- 96% of SVC sessions and 88% of FVC sessions were acceptable

**Proctored**: Conducted remotely via live video supervision

**Non-proctored**: Performed completely autonomously at home after participants completed and at least one proctored session

Peller et al., Front. Neurol., 2025

# **Looking Forward:** Expanding the ALS At-Home Respiratory Toolkit



# THANK YOU

**Questions?**

**Adam LaPrad, PhD**
Head of Product & Scientific Affairs
adam.laprad@zephyrx.com

modality.ai

# Self-Guided ALS Assessments


**Modality.AI, Inc., San Francisco, CA**

**David “DSO” Suendermann-Oeft, CEO**

d@modality.ai

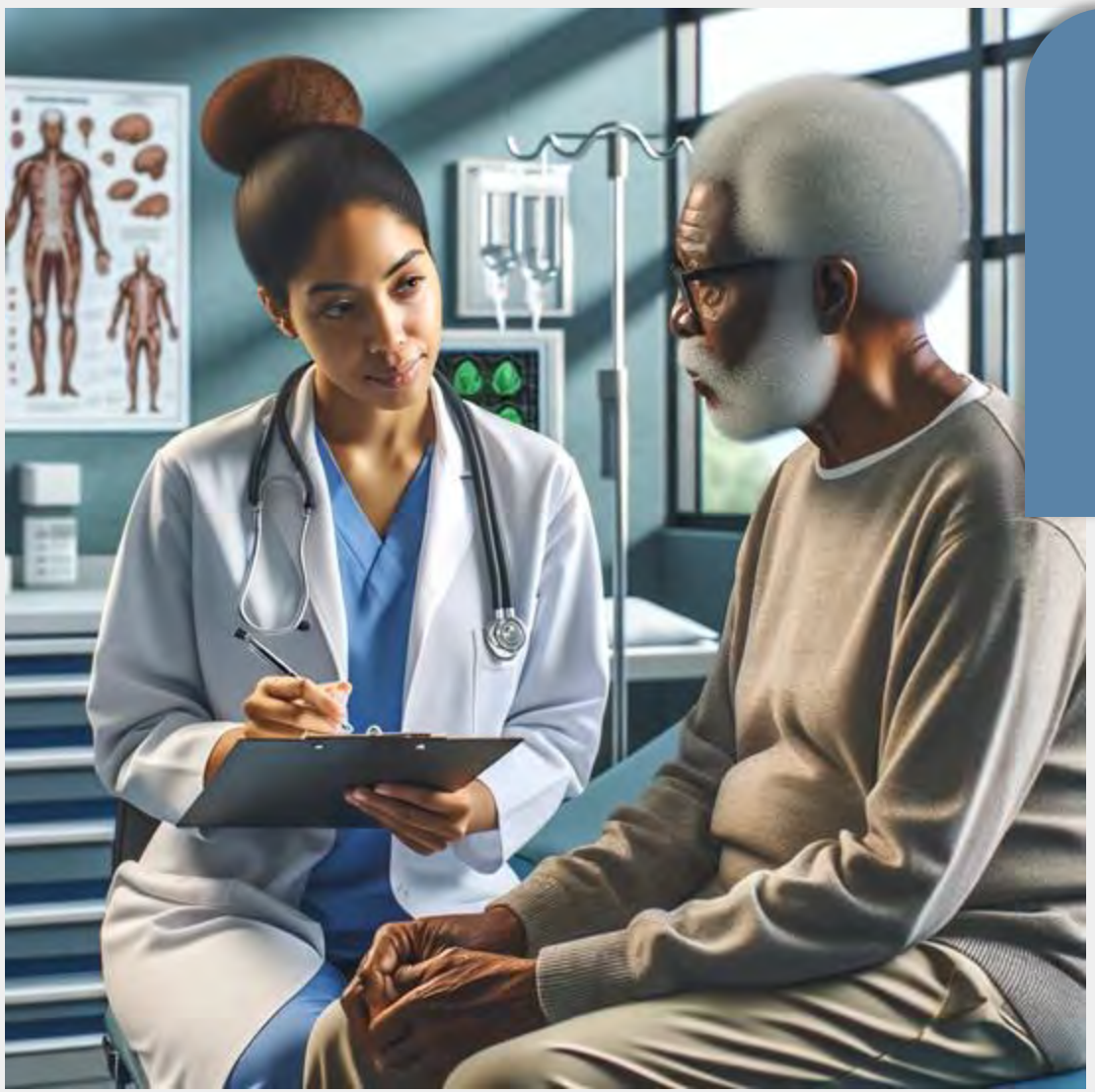
# Massive pain point in ALS trials

**4 out of 5 clinical trials fail overall**

**97% of ALS Phase 3 studies failed**

**Inadequate assessment is a key cause of failure**

# The “gold standard” of ALS assessment



**ALSFRS-R**

**In-clinic, infrequent**

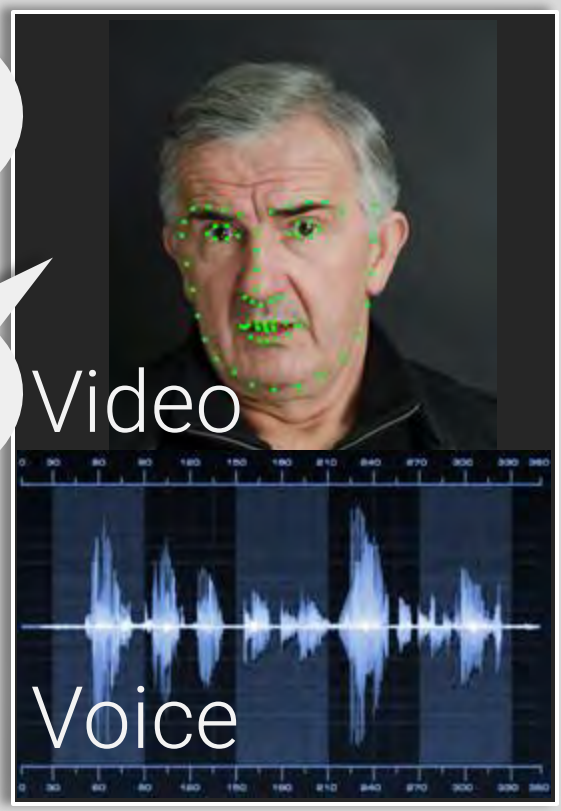
**Low sensitivity, low responsiveness**

# Tina assesses how ALS patients function and feel

## Virtual Guide

Tina

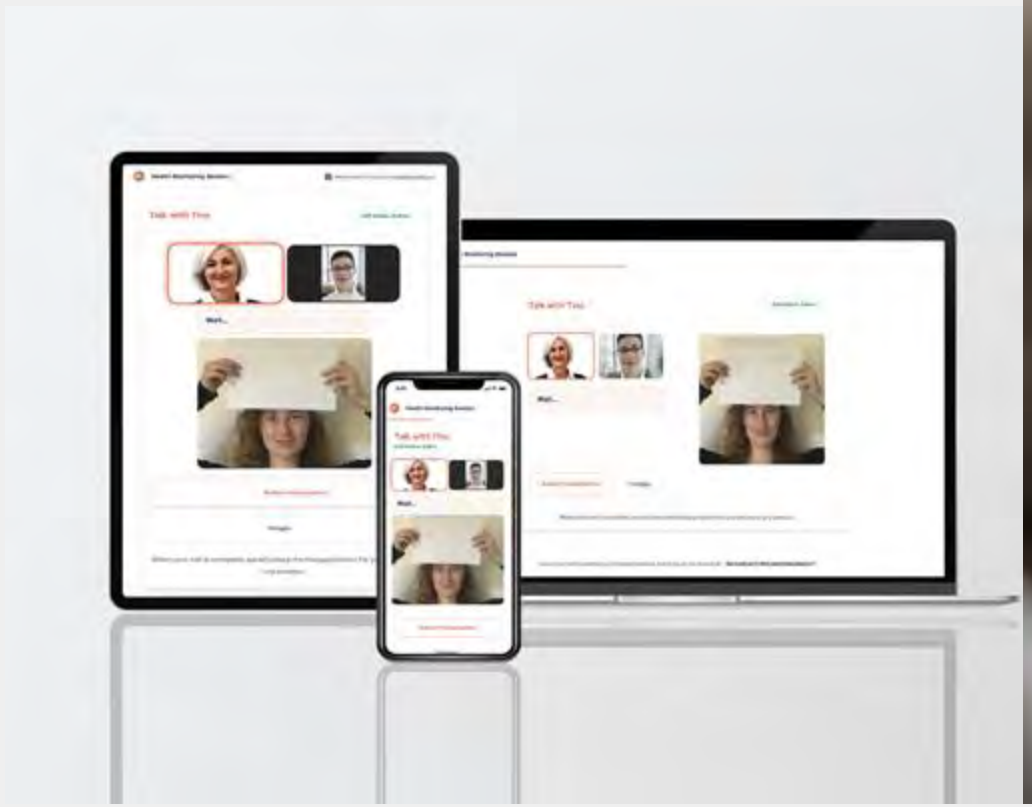
## Multimodal

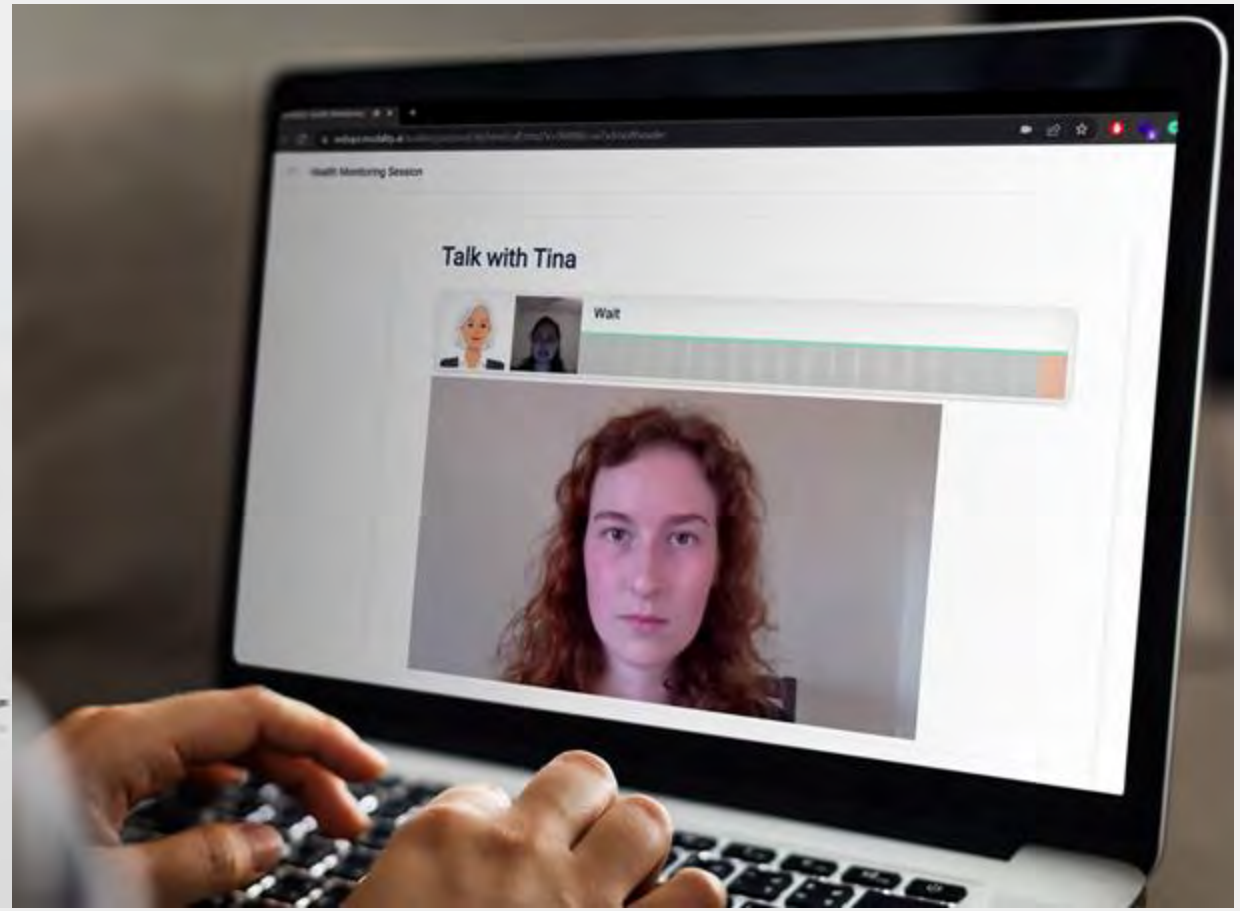



## Measures

- ❑ Speech
- ❑ Language
- ❑ Facial
- ❑ Body
- ❑ Cognitive
- ❑ PROP: Patient Report of Problems™

# Device-independent – no app to install





# Operational advantages

- ❏ No special hardware or software
- ❏ Works on tablets, phones, laptops, …
- ❏ Participants do not need to remember logins
- ❏ Remote self-administration guided by Tina
- ❏ Participants can continue to participate in later disease stages
- ❏ Data immediately available

# Customers and partners (selection from 30+)

PROTIBEA THERAPEUTICS INC.
cerevance
PhotoPharmics
eikönoklastes THERAPEUTICS
Trace Neuroscience
VERGE genomics
Dyne THERAPEUTICS
Canurta Therapeutics

ALS, Parkinson's, … (Phase 1, 2, 3)

TARGET ALS
MGH 1811
NIH

ALS

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

Parkinson's

J&J
VA U.S. Department of Veterans Affairs

MCI

Ametris

CNS

# Pipeline

**125** publications, **45** studies, **147** clinical sites, **17** countries, **18** languages/dialects
**78k** participants, **2.1M** recordings, **69** collaborator institutions, **21** patents filed

| Clinical R&D Area | Observational | Phase 1 | Phase 2 | Phase 3 | Publications |
|---|---|---|---|---|---|
| Parkinson's Disease | 5 | | 1 | 2 | 49 |
| ALS | 13 | 2 | 2 | | 29 |
| Schizophrenia | 1 | | 1 | | 15 |
| Neurocognition (MCI, …) | 3 | 1 | 1 | | 7 |
| Depression | 3 | | | | 5 |
| Autism | 1 | | 1 | | 5 |
| Huntington's Disease | 2 | | | | 7 |
| Multiple Sclerosis | 2 | | | | 1 |
| FSHD | | | 1 | | |
| Ataxia–Telangiectasia | 1 | | | | |
| Laryngeal Cancer | 1 | | | | |
| Lyme Disease | 1 | | | | |
| Modality Platform | Version 40 in Production | | | | 17 |

(updated September 30, 2025)

# ALS protocol & measures

| | | |
|---|---|---|
| **Speaking Duration/Rate (sec; words/sec)** | Captures articulation rate & timing of speech | Speech Measures |
| **Canonical Timing Alignment (CTA, %)** | Captures timing & intelligibility of speech | Speech Measures |
| **Percent Pause Time (PPT, %)** | Captures pausing characteristics of speech | Speech Measures |
| **Sustained Phonation Time** | Captures respiratory capacity | Speech Measures |
| **Jaw Velocity/Acceleration** | Captures orofacial movement characteristics | Facial Measures |
| **Lower Lip Velocity/Acceleration** | Captures orofacial movement characteristics | Facial Measures |
| **Clinical Symptom Probabilities (PROP)** | Captures patients problems in their own words | Verbatim Measures |

## Modality Protocol Stimulus Elements (6-10 minutes):

- ❑ Sustained Phonation
- ❑ Counting
- ❑ Diadochokinesis (DDK)
- ❑ Sentence Intelligibility Tasks
- ❑ Reading Passage
- ❑ Picture Description
- ❑ PROP

# Automated measures are more sensitive and responsive to longitudinal ALS progression than the ALSFRS-R

## Bulbar Onset

Slope = -0.1712 % points / week

Standard error of the slope = 0.0434 % points / week

Time to detect change > SE = 4 weeks

Time to detect a clinically-important change > 1 point on ALSFRS-R speech score = **4 weeks**

## Non-Bulbar Onset

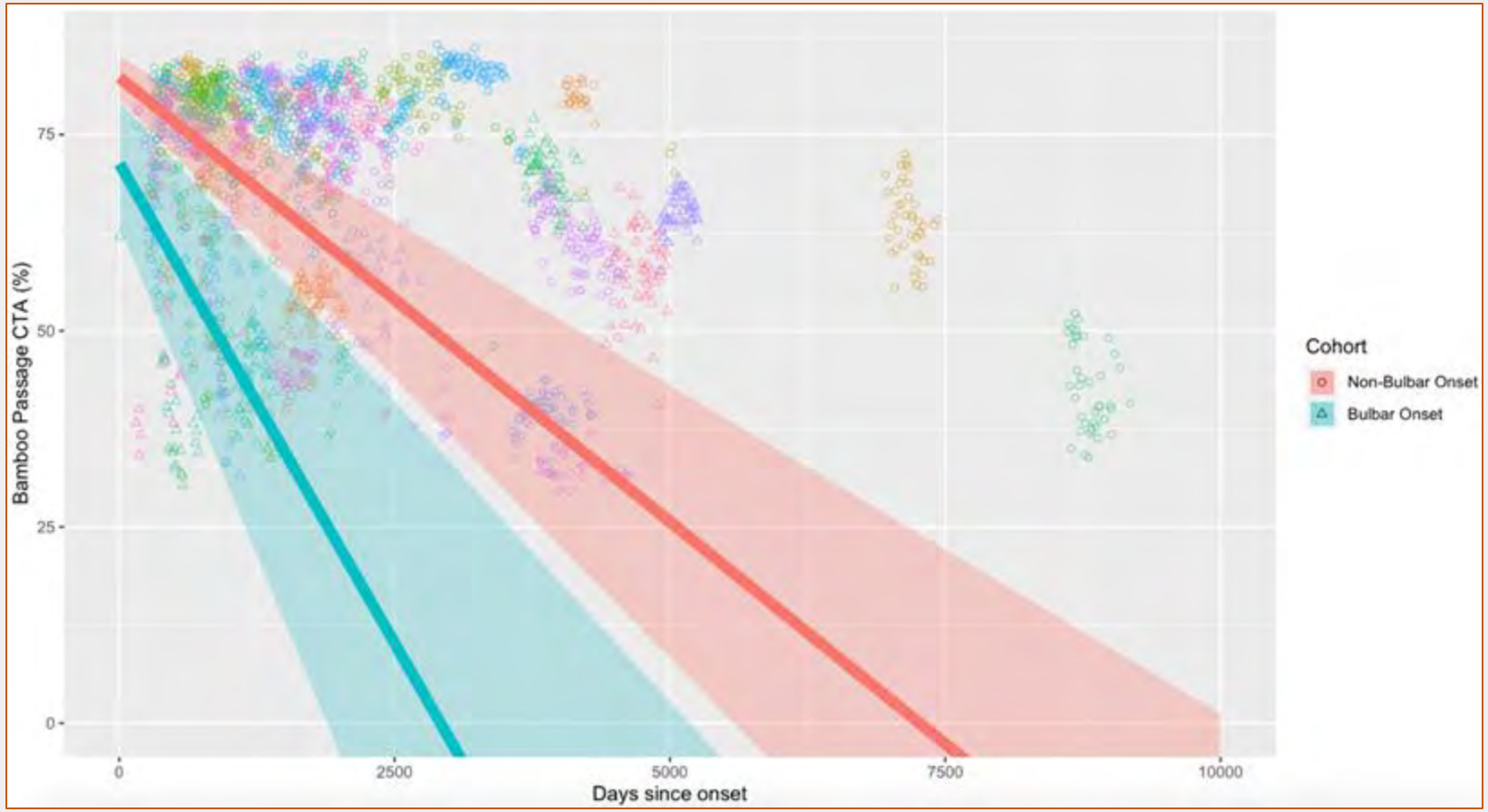
Slope (after accounting for learning effects) = -0.0793 % points / week

Standard error of the slope = 0.0206 % points / week

Time to detect change > SE = 5 weeks

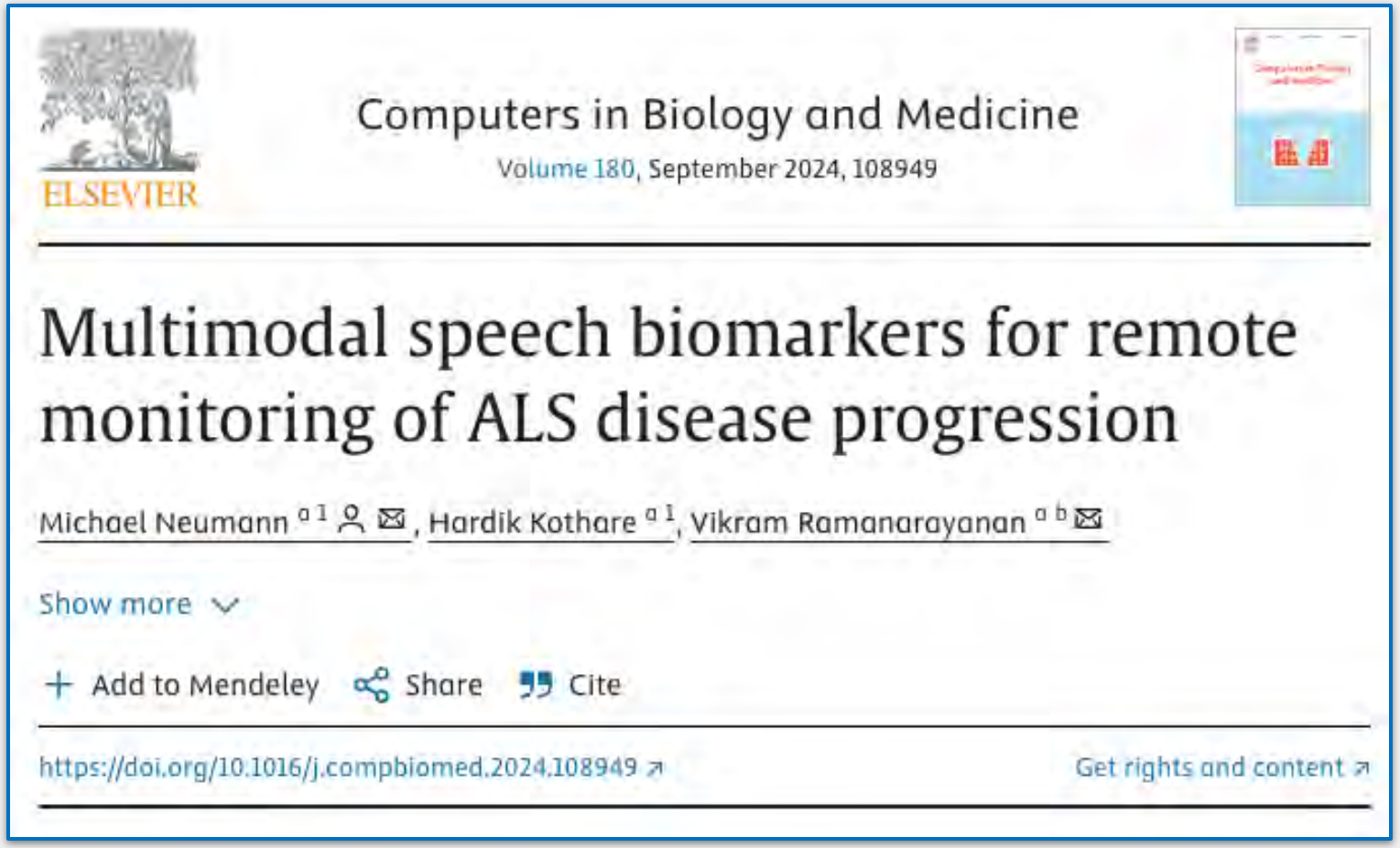
Time to detect a clinically-important change > 1 point on the ALSFRS-R speech score = **9 weeks**

## Canonical Word Timing Alignment (CTA, %) measures intelligibility




Growth curve models allow progress modeling

Kothare, H., et al. “Responsiveness, Sensitivity and Clinical Utility of Timing-Related Speech Biomarkers for Remote Monitoring of ALS Disease Progression.” Proc. Interspeech 2023, 2323-2327.



ELSEVIER

Computers in Biology and Medicine

Volume 180, September 2024, 108949

# Multimodal speech biomarkers for remote monitoring of ALS disease progression

Michael Neumann [a 1], Hardik Kothare [a 1], Vikram Ramanarayanan [a b]

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https://doi.org/10.1016/j.compbiomed.2024.108949

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- ❑ Findings stable with small samples
- ❑ Speech measures detected changes well before ALSFRS-R showed any change

# Takeaways

- ❑ Multimodal speech biomarkers can be reliably extracted from remote recordings
- ❑ 9 measures showed significant longitudinal changes in pALS
- ❑ Canonical Timing Alignment quickly detected clinically relevant changes

# Panel Discussion

**Adam LaPrad, PhD**
Head of Product and Scientific Affairs
*ZEPHYRx*

**Dr. Nadia Sethi**
Founder, Patient Advocate
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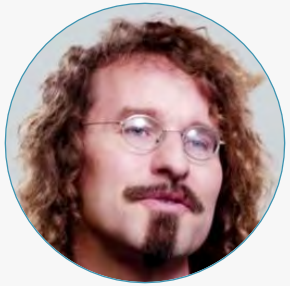

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Lead of DHT Solutions, Neuroscience
*Ametris (formerly ActiGraph)*

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# Thank You for Your Time

Scan
to watch Drs. Shu and Guo discuss how DHTs enable robust research data


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