

Thank you for joining the webinar!

We are admitting audience members from the waiting room.

**Please allow a few moments for the webinar to begin.**



# HEALEY ALS Platform Trial

## Community Q&A – August 28, 2025



## Healey & AMG Center

Sean M. Healey & AMG Center for ALS  
at Massachusetts General Hospital



The AMG Foundation

# Guest Speakers



**James Berry, MD, MPH**

Chief, Division of ALS and Motor Neuron Diseases  
Mass General Brigham Neurology



**Eric Macklin, PhD**

Assistant Investigator, Biostatistics  
Massachusetts General Hospital

# Partnership, progress, and pathways forward



ANNIVERSARY

*Thank You*



## COMMON PROTOCOL

Regimen G

Regimen F

Regimen E

Regimen D

Regimen C

Regimen B

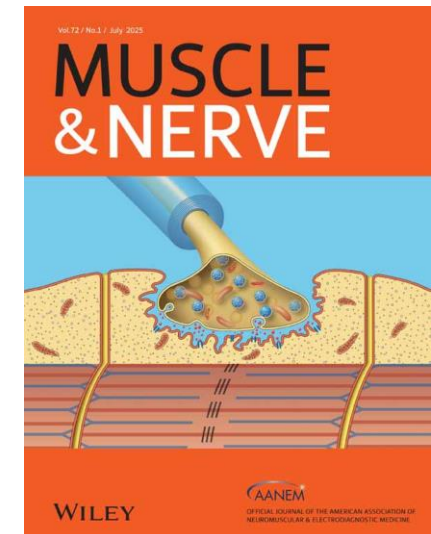
Regimen A

## Sharing our learnings

Operational Development and Launch of an Adaptive Platform Trial in Amyotrophic Lateral Sclerosis: **Processes and Learnings From the First Four Regimens of the HEALEY ALS Platform Trial**

First published: 26 May 2025

**Open Access**

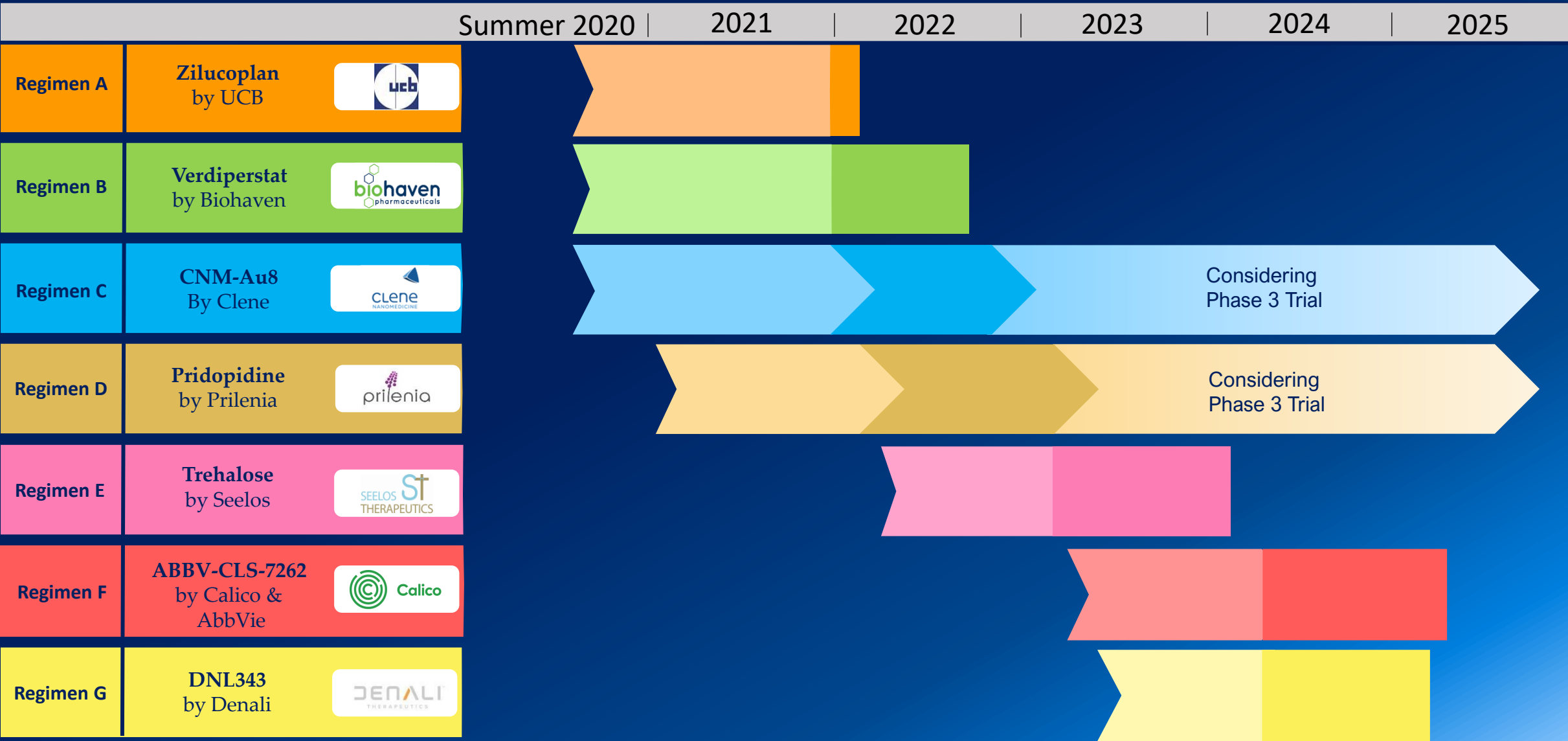


<https://onlinelibrary.wiley.com/doi/10.1002/mus.28442>



# The HEALEY ALS Platform Trial is designed to provide decisive answers and direction with efficient execution

HEALEY ALS Platform Trial



# Platform trials are a unique opportunity to advance science



**DNA** – whole genome sequencing



**Neurofilaments** –for all regimens



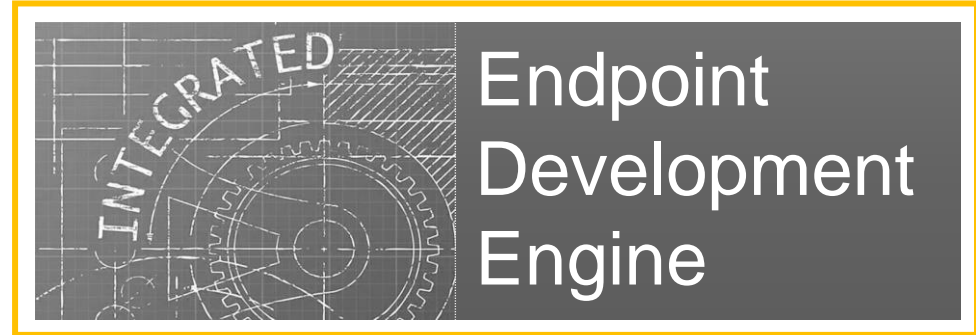
**Biomarkers** (Blood, CSF) – several drug-specific biomarkers



**Speech Analysis** – emerging digital biomarker



**Home Spirometry** – critical during the pandemic



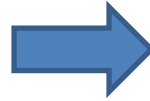
Additional biomarkers/outcome measures for upcoming regimens

# Focus on Digital Health Technologies in ALS Trials

What if...

...we could use digital devices to quantify people's function, hasten ALS drug discovery and reduce trial burden?

# There is Opportunity to Analyze Different Data

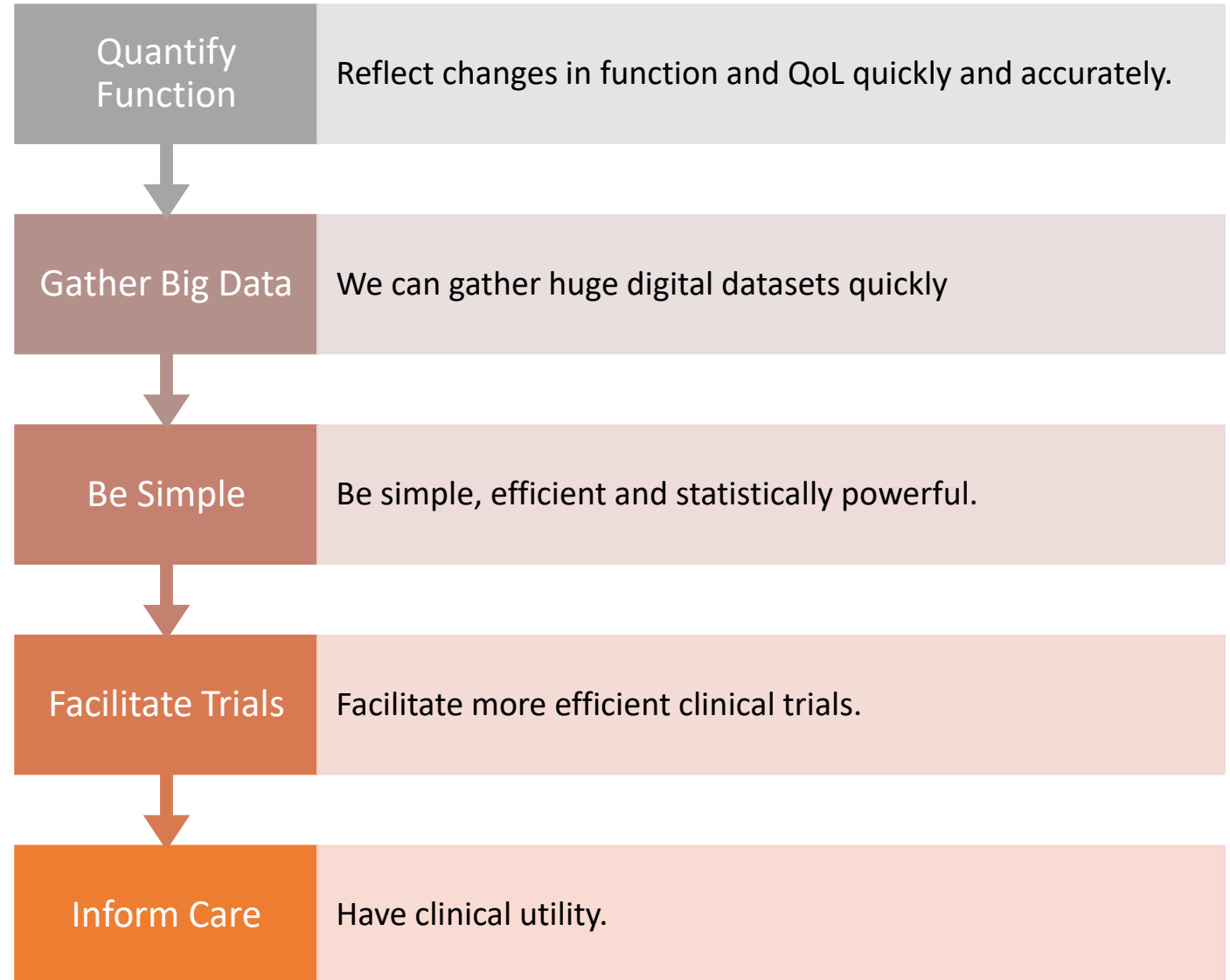


- Many additional scales and numerous unmeasured impacts of ALS

- We live in a data-rich world and should take advantage of that data.



# Digital biomarkers might:



# Where Digital Outcome Measures Stand for ALS



Researchers, PALS and regulators would like to move to digital outcome measures and some are close to acceptance



Goal: faster trials, less burden,  
more reflective of real-life impact

To be “worth” adopting, must improve  
on current outcomes



Steps to adopting digital outcomes

Gather data to show utility  
Feel comfortable with usability  
Understand change over time  
Regulatory considerations

# Home Spirometry in the Platform Trial



## Benefits

- critical during the pandemic
- mimics in-clinic spirometry almost exactly
- might be done more frequently

## Drawbacks

- all spirometry is subject to variability due to effort - ? Harder at home
- small differences in technique could impact results

- Included in the HEALEY ALS Platform Trial due to necessity
- Now we are analyzing to learn about home spirometry, itself

# Respiratory Function

## **The ability to breath is essential for life**

- Unfortunately, breathing becomes more difficult in ALS and is a central aspect of the disease
- Changes in respiratory function, the ability to breathe, track disease progression
  - Changes in respiratory function guide clinical care, e.g., need for assisted ventilation
  - Changes in respiratory function are also a useful endpoint in clinical trials, e.g., to see if an experimental drug slows progression and might extend life

## **Respiratory function was measured in two ways in Regimens A-D of the HEALEY ALS Platform Trial:**

- As slow vital capacity at clinical sites (in-clinic SVC), the gold standard
- As forced vital capacity at home (at-home FVC) using home spirometry





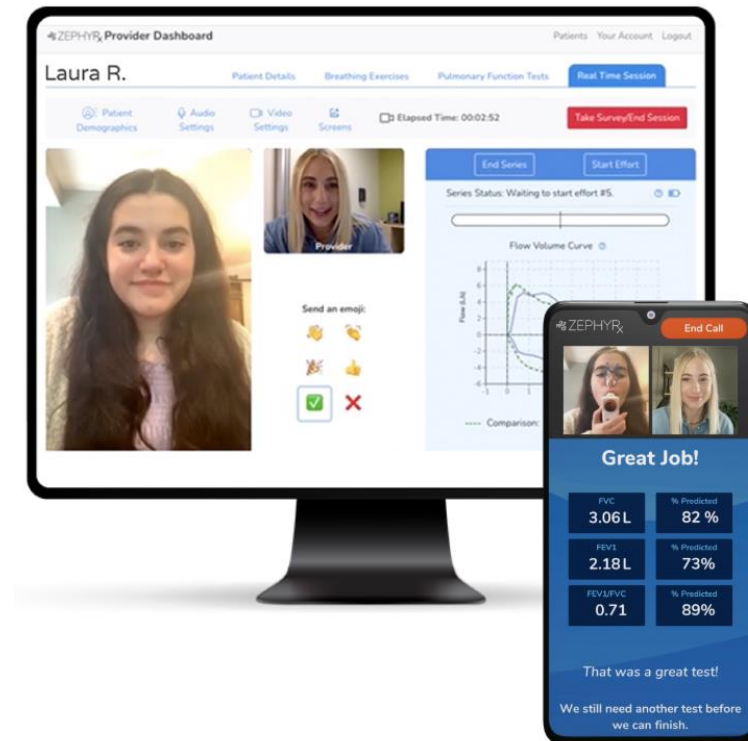
# Home Spirometry

## Home spirometry measures respiratory function remotely

- A small, handheld spirometer linked to a smartphone
- Video coaching by a site coordinator

## How accurate and informative are measurements of vital capacity when assessed by home spirometry?

1. Do in-clinic SVC and at-home FVC measurements match?
2. If someone were eligible for a trial based on at-home FVC, would they also be eligible by in-clinic SVC?
3. Do changes over time match and with equal precision?
4. If you track progression by at-home FVC, can you predict long-term survival as well as when you use in-clinic SVC?



# Data Used in Our Comparison

## We selected participants with matched in-clinic SVC and at-home FVC assessments with full or nearly full follow-up

- Regimen A-D participants
- In-clinic SVC and at-home FVC assessments completed less than 14 days apart
- Matched assessments at 3 or 4 visits completed at baseline and every 8 wks
- At-home FVC assessments reviewed by the BNI Outcomes Center and judged acceptable

## Characteristics

- Early in disease (typical of ALS trials)
- Slow progression rates (due to restriction to 3 or 4 visit completers)
- Average respiratory function 20% below normal (typical of ALS trials)

Characteristic	In-clinic SVC and At-home FVC <14 days apart at 3 or 4 visits (n = 166)
Sex, Male	111 (66.9%)
Race	
Asian	4 (2.4%)
Black	2 (1.2%)
White	159 (96.4%)
Ethnicity	2 (1.2%)
Age at baseline (yrs)	58.9±10.5 (23.6,79.0)
Bulbar onset	24 (14.5%)
Revised El Escorial criteria	
Possible	10 (6.0%)
Probable Lab-supported	42 (25.3%)
Probable	65 (39.2%)
Definite	49 (29.5%)
Riluzole use at baseline	138 (83.1%)
Edaravone use at baseline	36 (21.7%)
Nuedexta use at baseline	18 (10.8%)
Months from symptom onset	21.7±8.3 (2.7,37.7)
Months from diagnosis	11.1±7.2 (1.8,33.1)
Delta-FRS (pts/month)	0.63±0.40 (0.00,1.97)
Serum NfL at baseline (pg/mL)	72.8 (45.5,103)
ALSFRS-R Total score	36.1±5.8 (20.0,48.0)
ALSFRS-R Respiratory domain	10.5±2.2 (3.0,12.0)
In-clinic SVC (%-predicted)	80.0±17.2 (33.9,127)
At-home FVC (%-predicted)	81.0±18.9 (23.4,128)

Table 1. Participant characteristics.

[Values: n (%), mean±SD (range), or median (inter-quartile range)]

# 1. Do in-clinic SVC and at-home FVC measurements match?

## At-home FVC measurements are similar to in-clinic SVC

- In-clinic SVC and at-home FVC were well correlated,  $r = 0.80$  (95% CI 0.77 to 0.83)
- Systematic bias was  $<1$  %-predicted
- At-home FVC was a little more variable (estimates were a little lower on the low end and a little higher on the high end)

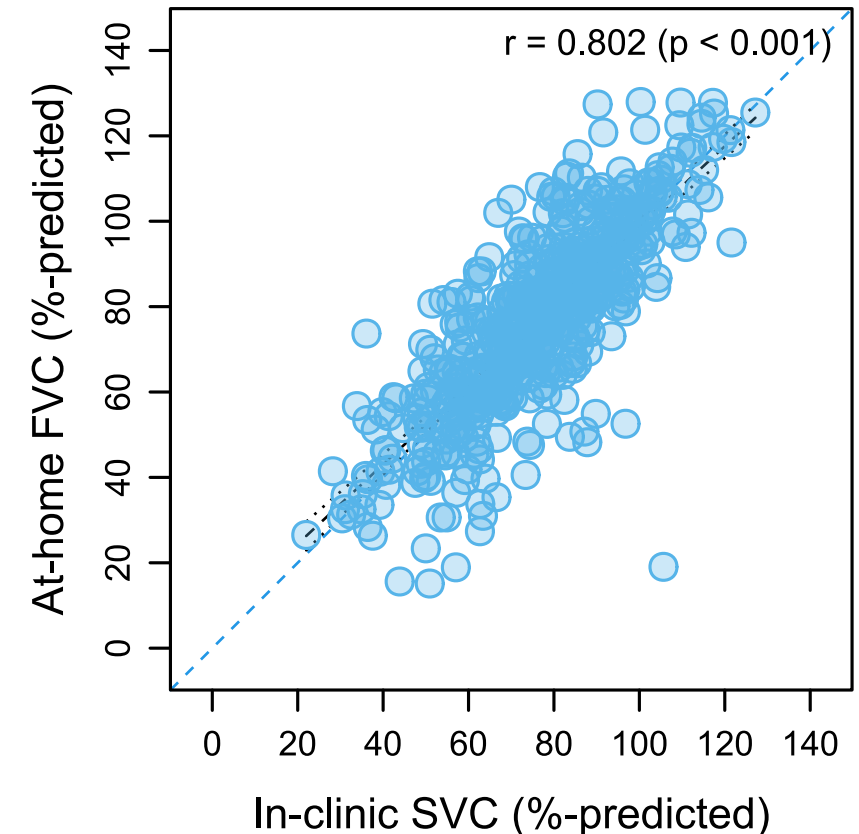


Figure 1. Scatterplot comparing in-clinic SVC and at-home FVC cross-sectionally. All assessments completed  $<14$  days apart.

## 2. Is eligibility based on at-home FVC the same as in-clinic SVC?

### At-home FVC measurements might exclude more people

- Overall accuracy was good, 87% (95% CI 83% to 90%)
- Most individuals above the cutoff at home would also be above the cutoff in clinic 92% (95% CI 88% to 95%)
- Some individuals might fall below the cutoff at home but above the cutoff in clinic 40% (95% CI 30% to 51%)

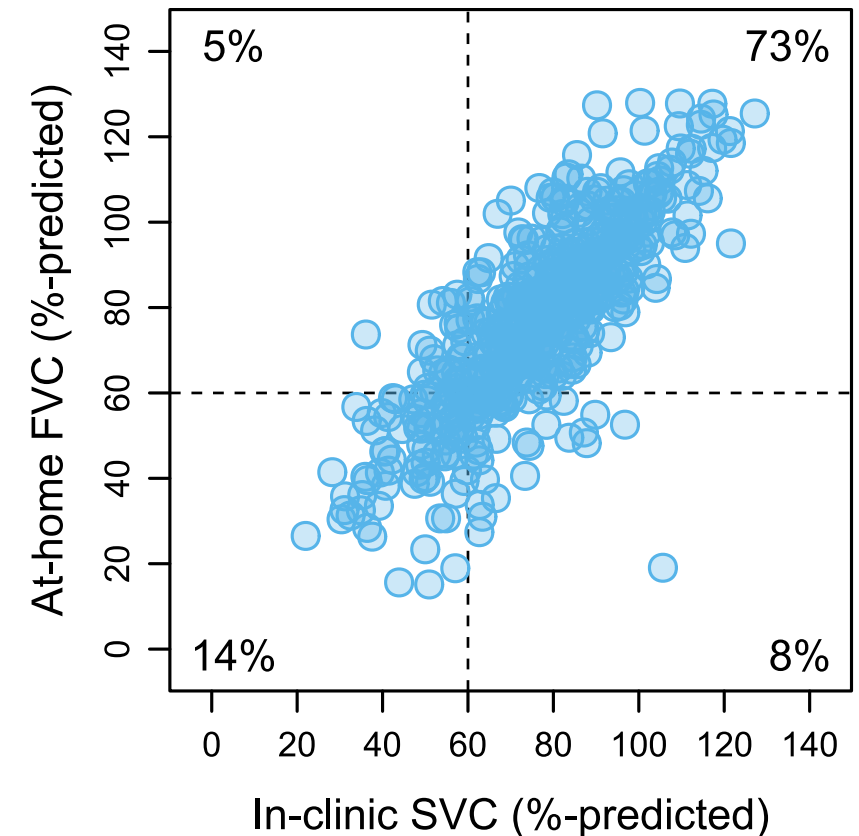


Figure 2. Scatterplot comparing in-clinic SVC and at-home FVC cross-sectionally. All assessments completed <14 days apart.



### 3. Do changes over time match and with equal precision?

**At-home FVC measurements change less over time and are slightly more variable from person to person**

- In-clinic SVC and at-home FVC were moderately correlated,  $r = 0.53$  (95% CI 0.41 to 0.63)
- Progression estimated by at-home FVC slopes was 28% slower
- At-home FVC slopes were a little more variable
- The relative precision of at-home FVC slopes was 44% lower

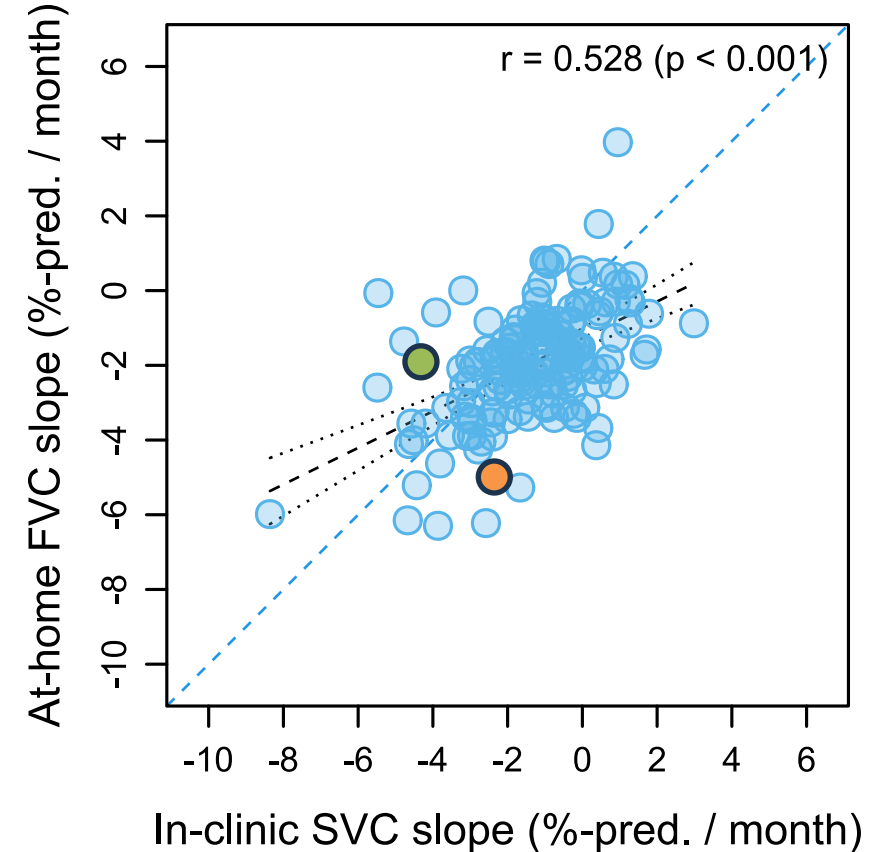


Figure 3. Scatterplot comparing in-clinic SVC and at-home FVC longitudinally. All assessments completed <14 days apart. Slopes estimated from unadjusted linear mixed models.

## 4. Does at-home FVC predict survival as well as in-clinic SVC?

### Change in both at-home FVC and in-clinic SVC predicted long-term survival

- Slopes of in-clinic SVC explained about 10% of the variation in long-term survival when in-clinic SVC was the only predictor
- Slopes of at-home FVC explained variation in long-term survival about 90% as well as in-clinic SVC when VC was the only predictor and about 60% as well when adjusting for other known predictors of survival

Endpoint	Covariates	Additional explained variation
In-clinic SVC	[none]	10.14%
	TRICALS	8.44%
At-home FVC	[none]	9.03%
	TRICALS	5.24%

Table 2. Variation in long-term survival times explained by in-clinic SVC or at-home FVC slopes from unadjusted and TRICALS-adjusted Cox proportional hazards models.

# Take-home Conclusions

- In-clinic SVC is still the gold standard measure of respiratory function
- Cons: At-home FVC is not a perfect substitute
- Pros: At-home FVC is much more convenient, reducing burden and allowing participation of many more PALS
- Understanding the trade-offs between accuracy and convenience will allow us to care for PALS more efficiently and to design better trials

# Patient Navigation

## Central resource for people living with ALS



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Two webinars  
per month

Sign up for  
ALS Link:



<https://bit.ly/3CqGbhb>

Register for  
webinars:



<https://bit.ly/3r6Nd2L>

September 2023

MON	TUE	WED	THU	FRI	SAT	SUN
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30					

**Upcoming Webinars (Thurs, 5:00- 5:30pm EST):**

**September 11 – Monthly EAP Discussion**

**September 25 – HEALEY ALS Platform Trial Placebo Retirement and Advisory Panel**