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Wearable device and smartphone data for tracking ALS disease progression

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Statement

The work presented in this presentation was conducted during my postdoctoral studies. The slides content and my talk do not represent the official stance or endorsement of my current employer, Takeda Pharmaceuticals, or any other organizations affiliated with Takeda Pharmaceuticals.

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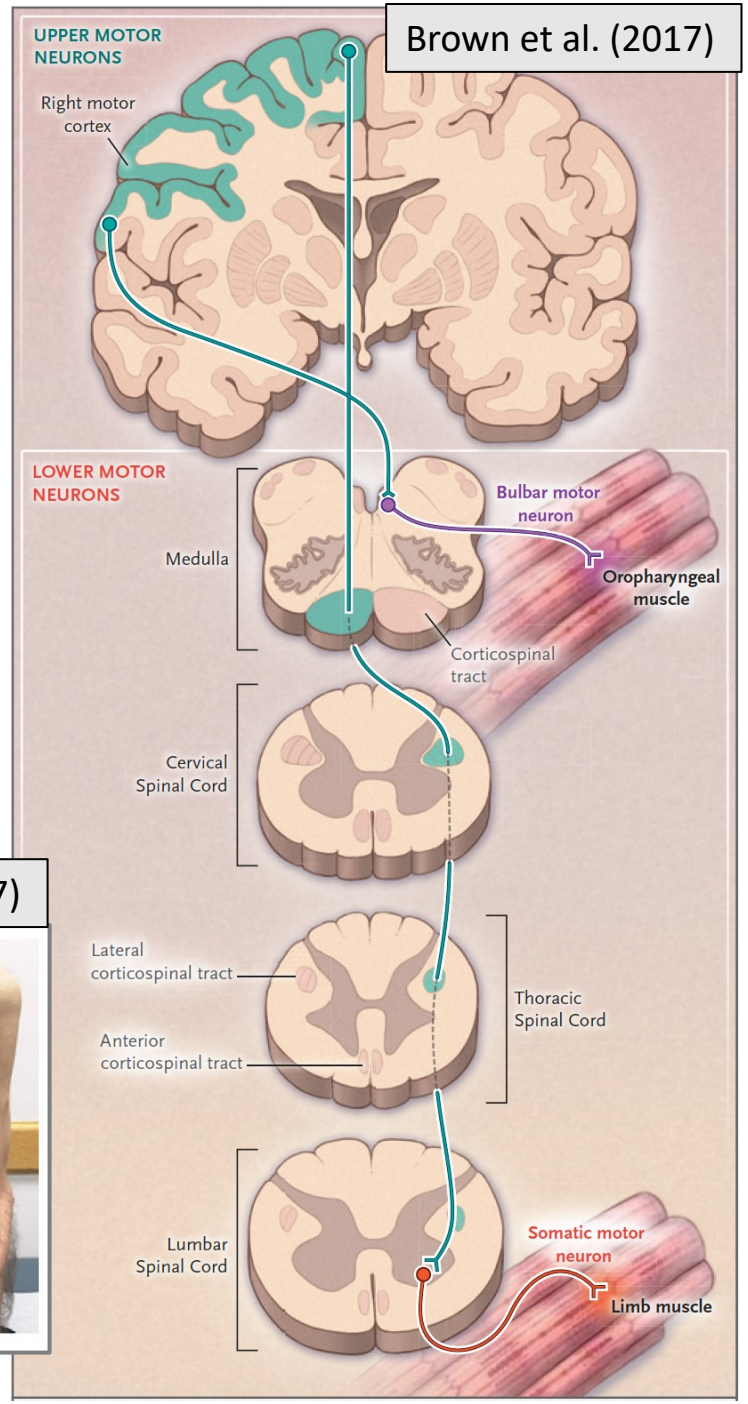
Outline

- [4 min] Background
- [4 min] Evaluating new avenues for outcome measures: smartphone apps and wearable devices
- [2 min] Discussion and future work

ALS

- Amyotrophic lateral sclerosis (ALS) -- fatal disorder characterized by progressive **loss of motor neurons in brain and spinal cord**
- In the US and Europe, cumulative lifetime risk is about **1 in 400**
- Symptom onset: 50-65y
- **Average life expectancy after diagnosis is 2-5y**
- 3 kinds of symptom onset: limb (70%), bulbar (25%), trunk/respiratory (5%)
- Symptom:
  - Progressive weakness and wasting of the limb and axial muscles
  - Bulbar (speech, swallowing)
  - Respiratory

Brown et al. (2017)



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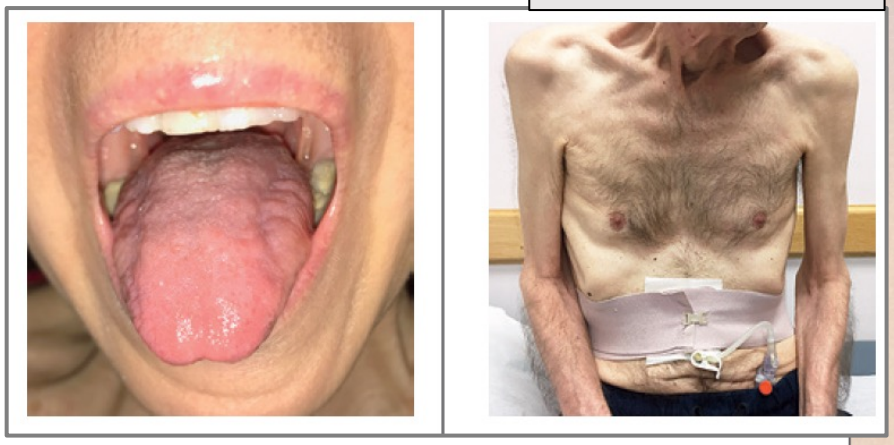


ALS FDA approved therapies

	Medicine	Mechanism of action	Brand name	Formulation	FDA approved
1	Riluzole	Decreasing the release of glutamate	Rilutek	Oral tablet	**1995**
			Tiglutik	Oral suspension	2018
			Exservan	Oral film	2019
2	Edaravone	Relieving the effects of oxidative stress	Radicava	Intravenous infusion	**2017**
				Oral suspension	2022
3	Sodium phenylbutyrate and tauroursodiol	Blocking stress signals in cells	Relyvrio	Oral suspension	**2022**
4	Tofersen	Reduction of SOD1 protein synthesis	Qalsody	Intrathecal injection	**2023**
5	Nuedexta	Regulating the signaling of glutamate and other neurotransmitters	Nuedexta	Oral tablet	2011

Primary endpoints in clinical trials for ALS

- **ALS Functional Rating Scale-Revised (ALSFRS-R)** is most commonly used primary endpoint in clinical trials for ALS
- Rating scale for monitoring disability progression in patients with ALS
- **12-item, 0-4 points/item scale** (total score range 0-48)
- Assess the fine motor, gross motor, bulbar, and respiratory function
- Traditionally staff-administered
- Limitations: it is ordinal, may not adequately reflect changes in certain areas

https://alstreatment.com/als-functional-rating-scale/

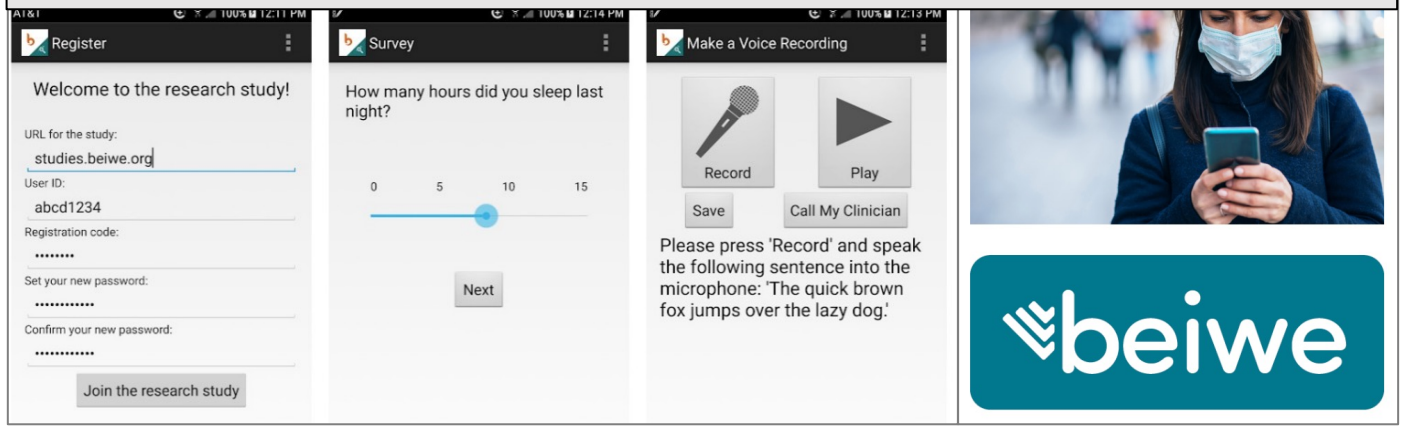
New avenues for outcome measures: mobile apps and wearable devices

- Remote study, N=40 subjects with ALS, followed for 6 months
- Sample: median [range] age -- 63 [34-98], baseline ALSFRS-R -- 33 [11-47]
- Staff-administered ALSFRS-R by televisit
- Digital technology:
  - All N=40: **Beiwe smartphone application** to collect self-entry ALSFRS-R
  - N=20 wrist-worn **ActiGraph Insight Watch**
  - N=20 ankle-worn **Modus StepWatch 4**

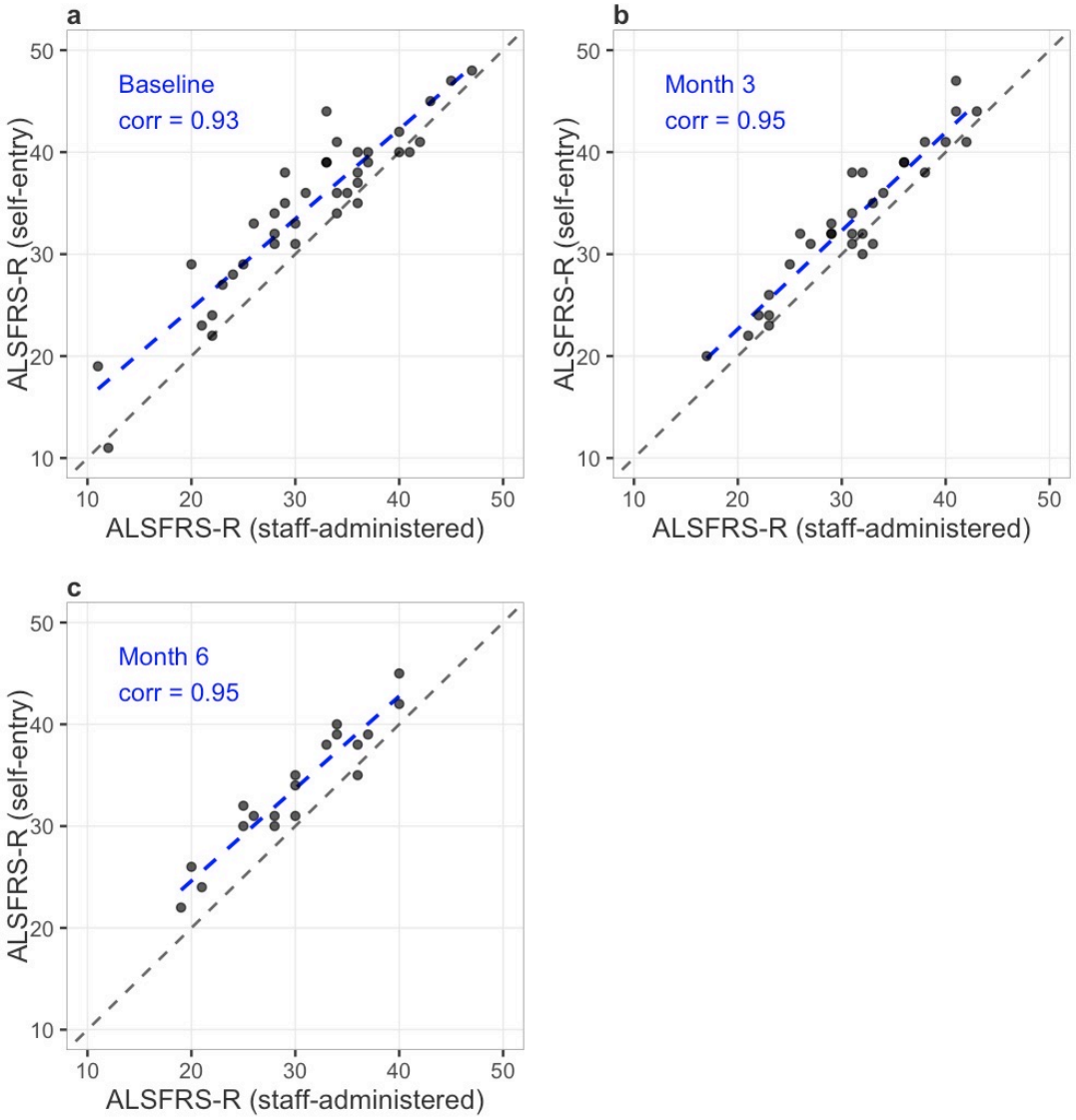
ActiGraph Insight Watch

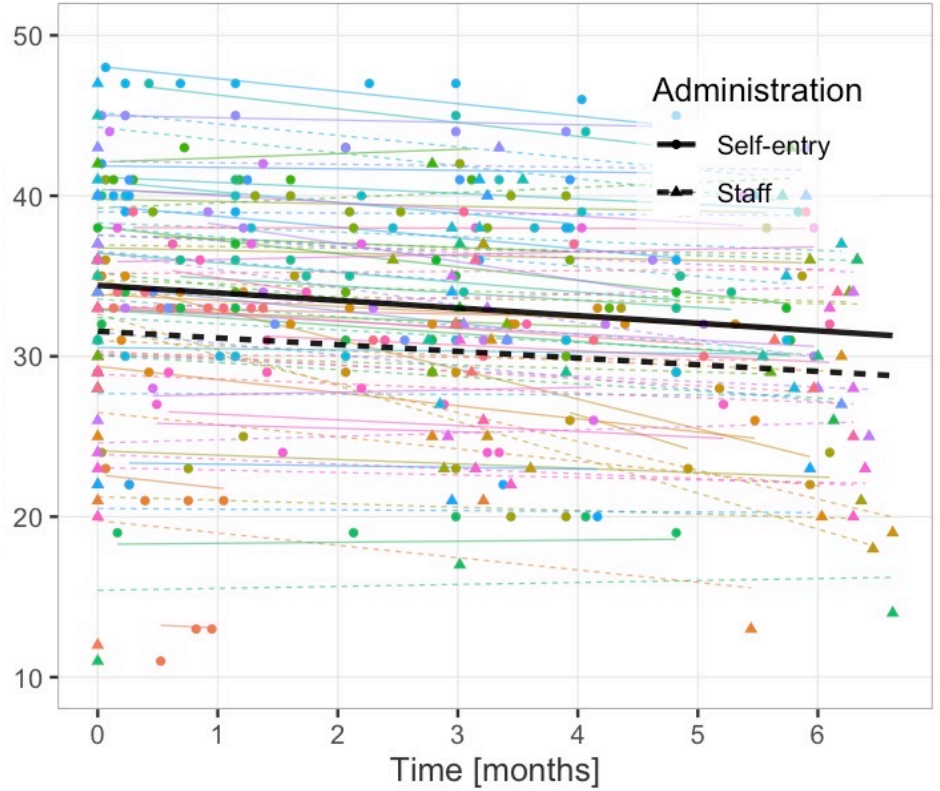
Modus StepWatch 4

Beiwe smartphone application (Harvard University, Onnela Lab)



Smartphone self-reported ALSFRS-R correlates highly with staff-administered





- Baseline **smartphone self-reported ALSFRS-R** was **34.3** and monthly rates of decline was **-0.48** (95% CI: [-0.63 -0.32])
- Significantly higher (2.86 [2.26, 3.47]) than staff-administered ALSFRS-R at baseline; monthly rates did not differ significantly

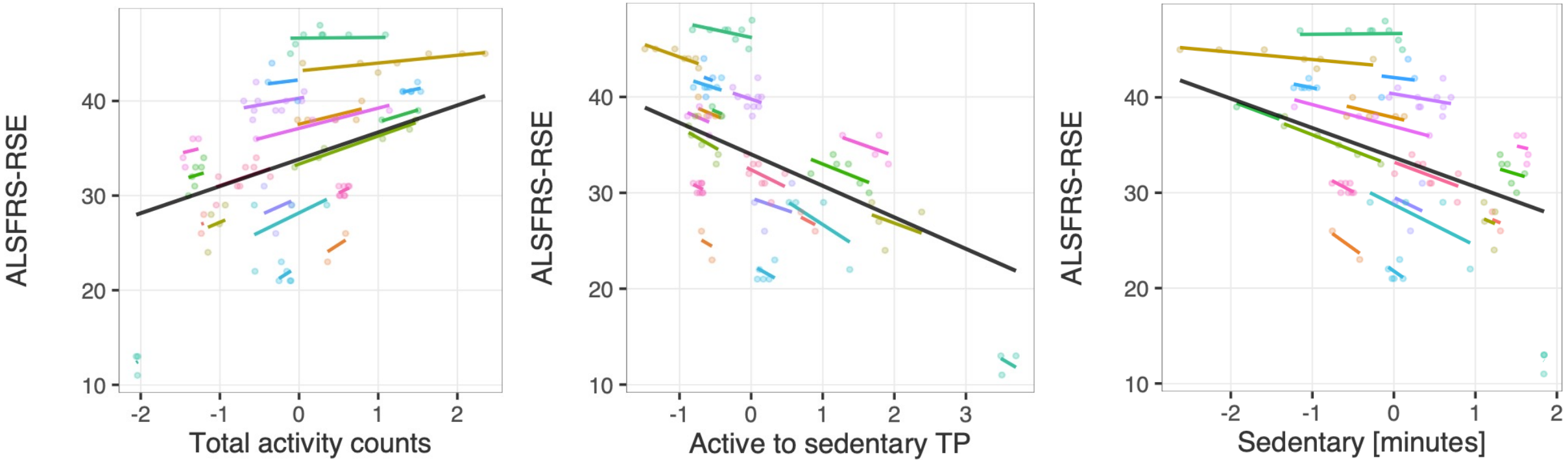
Wearable data-derived daily measures of physical activity showed significant change over time

Out of 32 measures considered, **23 measures showed significant change over time (**14/20 ActiGraph and 9/12 Modus)

	Device	Daily measure	Baseline est. [95% CI]	Monthly change est. [95% CI] (*p*)
1	ActiGraph	Total activity counts	1362438 [1046388, 1678489]	-58631 [-102202, -15059] (0.012)
2	ActiGraph	log(total activity counts)	13.90 [13.50, 14.31]	-0.046 [-0.078, -0.013] (0.011)
3	ActiGraph	Active to sedentary transition prob.	0.389 [0.299, 0.479]	0.009 [0.003, 0.014] (0.003)
4	ActiGraph	Sedentary to active transition prob.	0.074 [0.057, 0.091]	-0.003 [-0.006, 0.000] (0.028)
5	ActiGraph	Non-sedentary [minutes]	271.4 [200.6, 342.2]	-12.88 [-22.23, -3.530] (0.010)
(...)				
21	Modus	Total steps	1871 [1137, 2605]	-57.79 [-89.26, -26.32] (0.001)
22	Modus	Steps recorded/minute - 95th perc.	25.92 [21.19, 30.65]	-0.533 [-1.015, -0.052] (0.032)
23	Modus	Steps recorded/minute - mean	9.170 [7.050, 11.29]	-0.149 [-0.265, -0.034] (0.015)
24	Modus	Time % with 1-15 steps recorded/min.	9.395 [7.334, 11.46]	-0.187 [-0.315, -0.060] (0.006)
25	Modus	Time % with 16-40 steps recorded/min.	2.743 [1.451, 4.036]	-0.120 [-0.182, -0.057] (0.001)

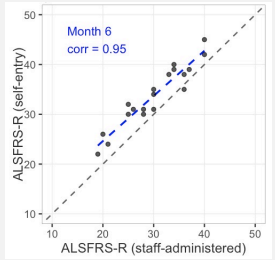
Wearable data-derived daily measures were significantly associated with smartphone self-reported ALSFRS-R

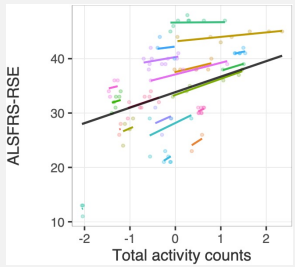
Out of 32 measures considered, **14 measures showed significant change over time & were significantly associated with smartphone self-reported ALSFRS-R (**12/20 ActiGraph and 2/12 Modus)



Discussion and future work

- Affirms the feasibility and utility of remote monitoring with apps and wearable devices
- Other considerations
  - Challenges with remote digital data collection
  - Interpreting measures in the absence of context
  - Evaluating scenarios of different data collection protocols
- Further research areas
  - Measures sensitivity depending on ALS onset
  - Incorporation of digital outcome measures into interventional clinical trials





- Johnson, S.A.*, Karas, M.*, Burke, K.M. et al. Wearable device and smartphone data quantify ALS progression and may provide novel outcome measures. *npj Digit. Med*. 6, 34 (2023). https://doi.org/10.1038/s41746-023-00778-y

Upcoming work:

- Straczkiewicz, M., Karas, M., Johnson, S.A. et al. Forearm movements as digital biomarkers in people with ALS.
- Karas, M.*, Olsen, J.*, Straczkiewicz, M. et al. Passively collected smartphone sensor data tracks ALS disease progression.

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