Developing Digital Measures of Function using Wearable Sensors for Alzheimer's Disease

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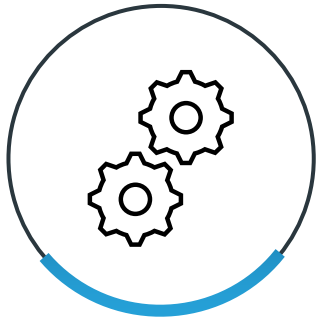
About VivoSense

VivoSense **develops and validates** digital clinical measures and provides **end-to-end services and solutions** for their delivery in **regulated** clinical trials.

Science Operations



Science R&D

Develop and validate
context- and population-specific
digital clinical measures

Software

Functional Independence Matters to Patients Alzheimer's Disease

AD is associated with cognitive and physical changes that affect day-to-day functioning and disability.

Dubbelman et al., 2020, *Alzheimers Res Ther*
Bruderer-Hofstetter et al., 2022, *BMC Geriatr*

Patients with AD and their caregivers consistently report the importance of **maintaining the ability to function independently**.

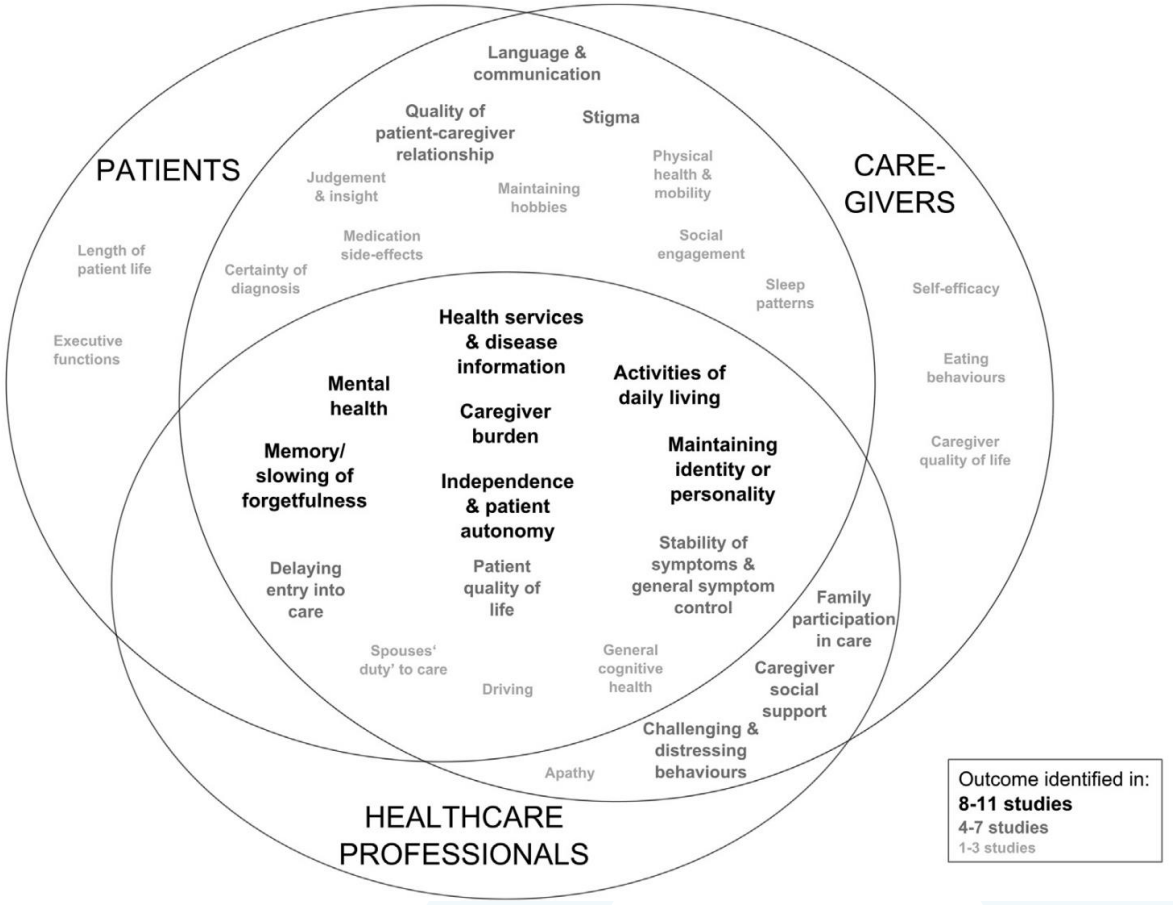


Figure from Tochel et al., 2019,
Alzheimers Dement Diagn Assess Dis Monit

Established Approach to Measuring Function in Alzheimer's Disease

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Lecanemab in Early Alzheimer's Disease

van Dyck CH et al. DOI: 10.1056/NEJMoa2212948

CLINICAL PROBLEM

Some evidence suggests that amyloid removal slows the progression of Alzheimer's disease. Lecanemab, an anti-amyloid monoclonal antibody with high affinity for soluble amyloid protofibrils, is being tested in early Alzheimer's disease.

CLINICAL TRIAL

Design: A phase 3, multicenter, double-blind, randomized, placebo-controlled trial assessed the efficacy and safety of lecanemab in patients 50 to 90 years of age with early Alzheimer's disease.

Intervention: 1795 participants in North America, Europe, and Asia were assigned to receive intravenous lecanemab (10 mg per kilogram of body weight every 2 weeks) or placebo. The primary efficacy end point was the change in the score on the Clinical Dementia Rating–Sum of Boxes (CDR-SB) from baseline, with higher scores indicating greater impairment.

RESULTS

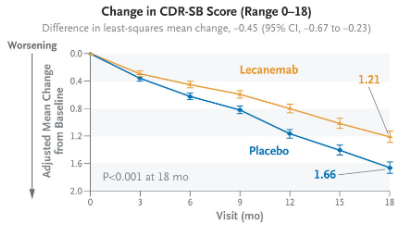
Efficacy: At 18 months, mean CDR-SB scores had worsened in both groups. The mean change in CDR-SB score was smaller (indicating less cognitive and functional decline) in the lecanemab group.

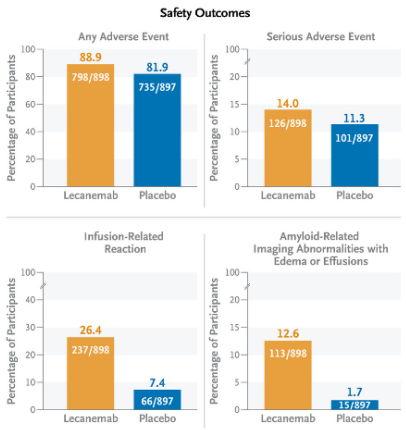
Safety: Overall incidences of adverse events were similar in the two groups. The most common adverse events in the lecanemab group included infusion-related reactions and amyloid-related imaging abnormalities with edema or effusions.

LIMITATIONS AND REMAINING QUESTIONS

- Longer-term follow-up is needed; an open-label extension study is ongoing.
- The trial was conducted during the Covid-19 pandemic and, as a result, faced challenges including missing data, missed doses, delayed assessments, and intercurrent illnesses.
- Occurrences of amyloid-related imaging abnormalities may have led to unblinding of participants and investigators.

Links: Full Article | NEJM Quick Take | Editorial

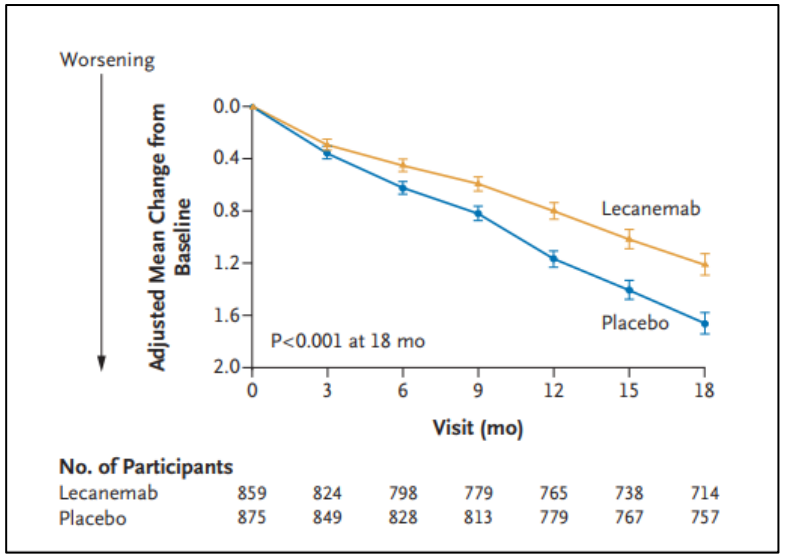




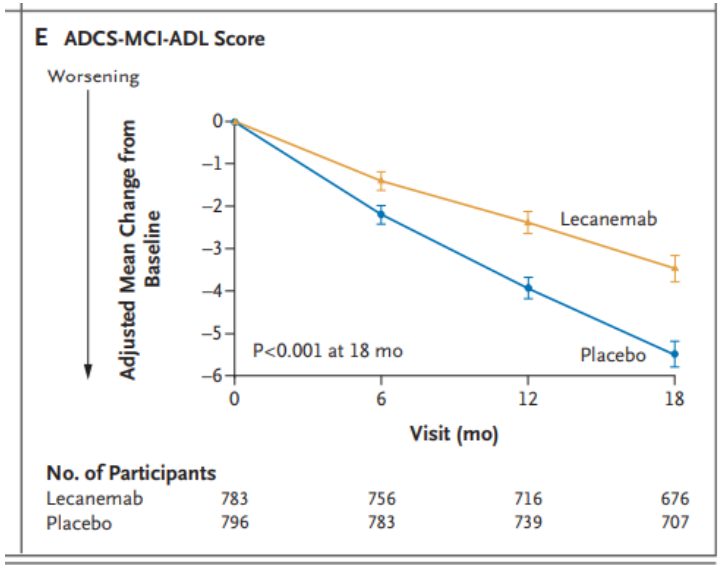
CONCLUSIONS

In patients with early Alzheimer's disease, lecanemab was associated with moderately less decline on measures of cognition and function than placebo over a period of 18 months.

Primary endpoint: CDR Sum of Boxes



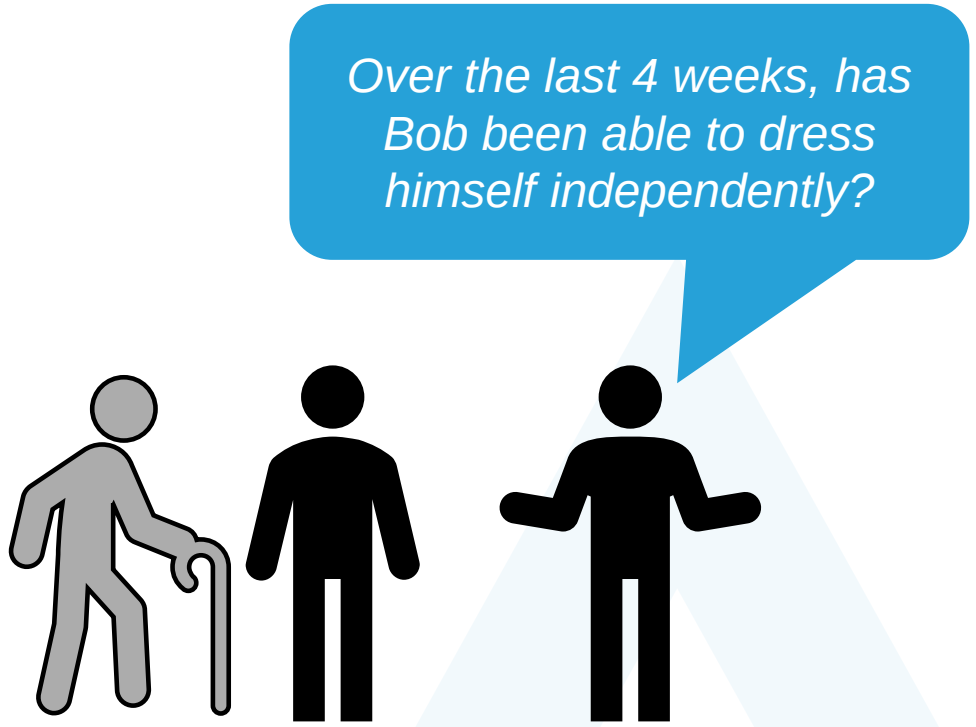
ADCS-MCI-ADL Score



Figures from van Dyck et al., 2023, *NEJM*

Limitations of Existing Methods of Function

- Episodic
- Subjective to recall and rater bias
- Burdensome and dependent on informant reports
- **Do not reflect patients' lived experience**
  - Assessed in clinic settings
  - Do not capture everyday functional challenges



Importance of Patients' Lived Experiences

FDA has shifted drug development approaches towards the patient

Patient Focused Drug Development (PFDD)

Develop drugs that improve aspects of life that matter to patients

Problem

There is an **unmet need** to develop new methods to **capture aspects of functioning** that **matter to patients** with Alzheimer's disease.

Opportunities for Wearable Actigraphy Sensors in AD

- Can capture many measures of physical behavior carried out in daily life, including walking
- Enable low-burden, continuous, and passive assessments of function in home environments
- Complement subjective ratings of function
- Detect treatment effects more efficiently with ecologically relevant endpoints

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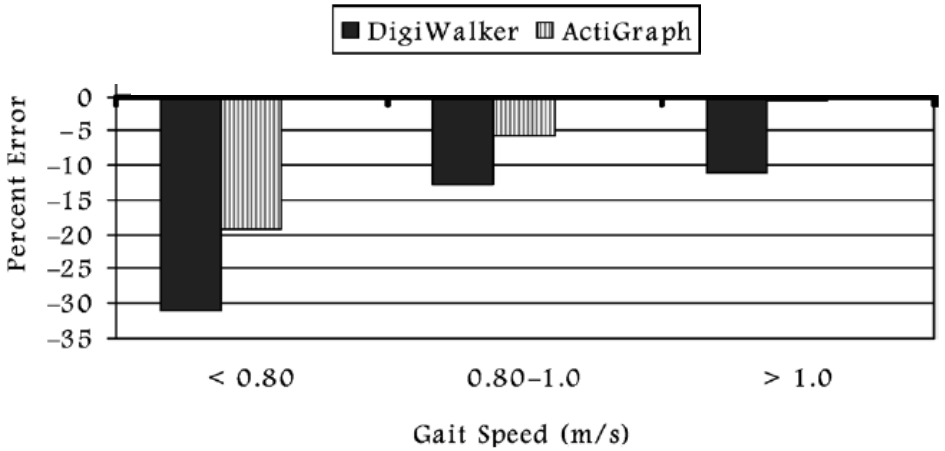
Assessing Walking Behaviors in AD with Actigraphy Sensors

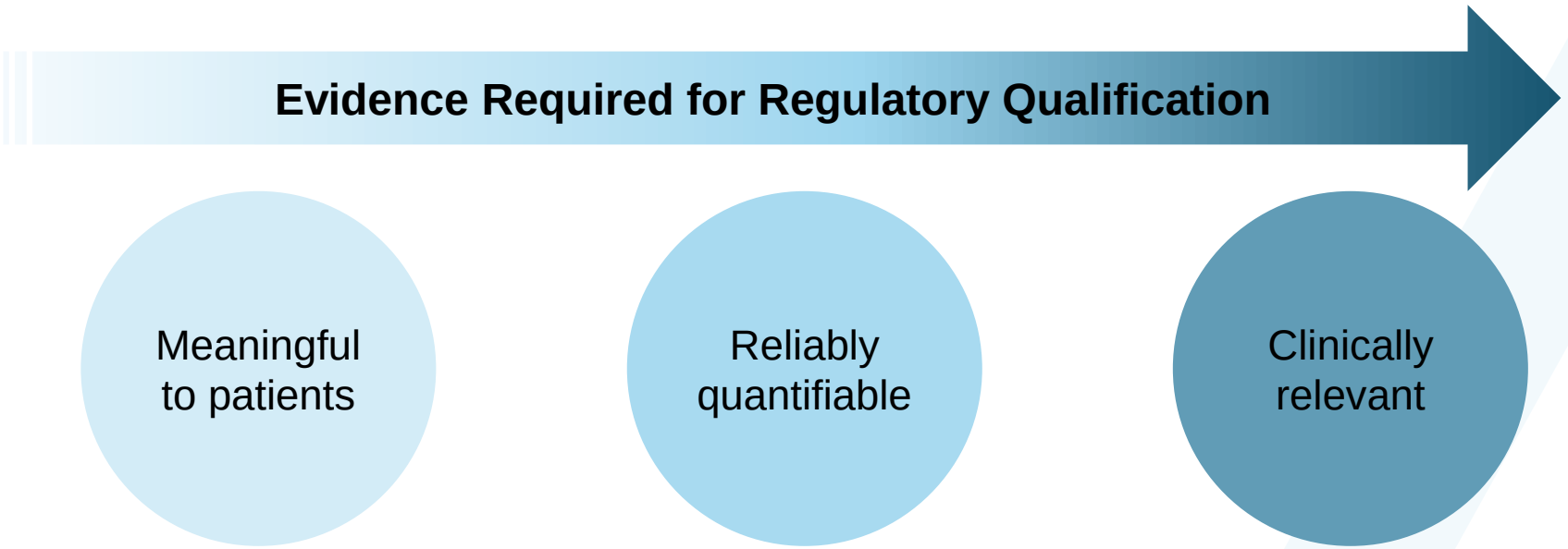
- Walking behaviors are central to functional independence.
- Most algorithms to derive walking behavior have been developed in healthy populations.
- Existing algorithms underestimate steps in individuals with slower gait, such as those with Alzheimer's disease



Adapted from *Storti et al., MMSE, 2008*

Long-Term Research Goals of VivoSense Science R&D

- Obtain regulatory qualification of a real-world digital measure of function in Alzheimer's disease
  - Well-defined and reliable assessment
  - Accepted by FDA for regulatory decision making



MassAITC Pilot Study Specific Aims

Aim 1

Develop and validate novel methods to detect walking behaviors from inertial sensors

Aim 2

Validate clinical meaningfulness of digital biomarkers in real-world environments

Aim 3

Evaluate the feasibility and acceptability of wearable sensors in real-world environment

The Team: Multi-disciplinary Academic-Industry Partnership

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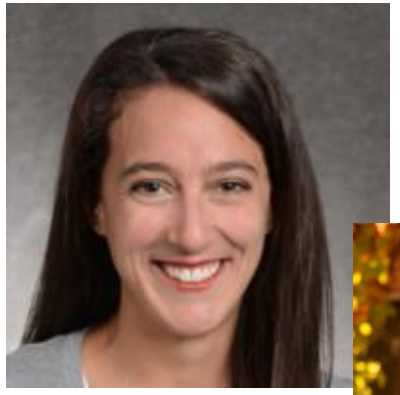
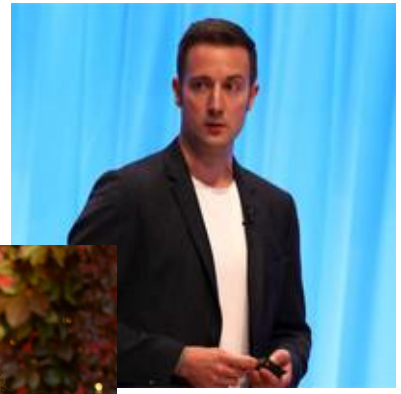
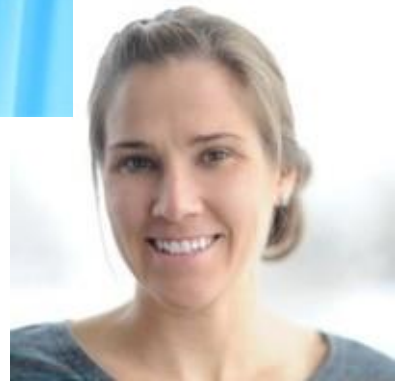


Jen Blankenship, PhD

Shelby Bachman, PhD



Ieuan Clay, PhD



Kate Lyden, PhD

UMass Amherst

Michael Busa, PhD

Corinna Serviente, PhD

Participants

Twenty older adults with (n=10) and without (n=10) Alzheimer's disease

Inclusion/Exclusion Criteria (all participants)

- ≥ 65 years
- Free from other types of dementia, traumatic brain injury or cerebral vascular stroke

Inclusion/Exclusion Criteria (patients with Alzheimer's disease)

- Self-reported diagnosis of mild Alzheimer's disease

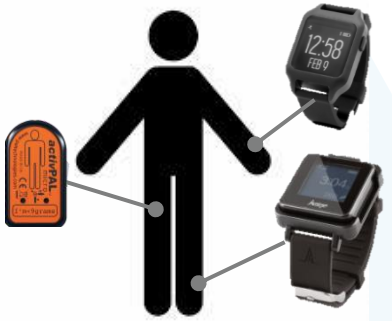
Study Design: Aim 1

MOTION CAPTURE LABORATORY

- Multiple assessments of walking behaviors captured while wearing inertial sensors (ActiGraph GT9x and CPIW, activPAL
- Truth data captured using 9-camera motion capture system

ALGORITHM DEVELOPMENT

- Develop machine learning algorithms to derive measures of real-world walking behavior in Alzheimer's disease

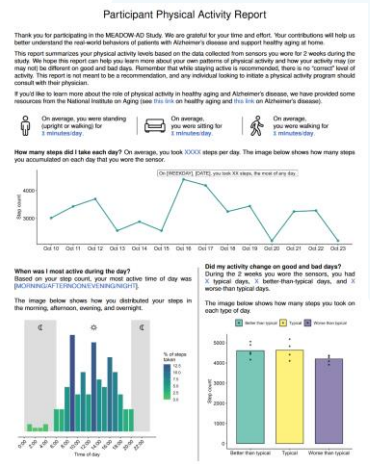


Study Design: Aim 2 and 3

REAL-WORLD MONITORING

- **At-home**
  - Participants will wear monitors on wrist and thigh for 2 weeks to assess how patients function at home
  - Evaluate group differences in real-world walking behaviors

- **After wearing monitors**
  - Participants complete wearable sensors feasibility and acceptability questionnaire
  - Wearable sensor data summary report generated and provided to participants
  - Questionnaire deployed to evaluate meaningfulness of data


Participant Physical Activity Report

Thank you for participating in the MEADOW AD Study. We are grateful for your time and effort. Your contributions will help us better understand the real-world behaviors of patients with Alzheimer's disease and support healthy aging at home.

This report summarizes your physical activity levels based on the data collected from sensors you wore for 2 weeks during the study. We hope this report can help you learn more about your own patterns of physical activity and how your activity may (or may not) be different on good and bad days. Remember that while staying active is recommended, there is no "correct" level of activity. This report is not meant to be a recommendation, and any individual looking to initiate a physical activity program should consult with their physician.

If you'd like to learn more about the role of physical activity in healthy aging and Alzheimer's disease, we have provided some resources from the National Institute on Aging (see this link on healthy aging and this link on Alzheimer's disease).

On average, you were standing (upright or walking) for ___ minutes/day.

On average, you were sitting for ___ minutes/day.

On average, you were walking for ___ minutes/day.

How many steps did I take each day? On average, you took XXXX steps per day. The image below shows how many steps you accumulated on each day that you were the sensor.

On [WEEKDAY], [DATE], you took XX steps, the most of any day.

Step count

Oct 10 Oct 11 Oct 12 Oct 13 Oct 14 Oct 15 Oct 16 Oct 17 Oct 18 Oct 19 Oct 20 Oct 21 Oct 22 Oct 23

When was I most active during the day?

Based on your step count, your most active time of day was [MORNING/AFTERNOON/EVENING/NIGHT].

The image below shows how you distributed your steps in the morning, afternoon, evening, and overnight.

% of steps taken

Time of day

Did my activity change on good and bad days?

During the 2 weeks you were the sensors, you had X typical days, X better-than-typical days, and X worse-than-typical days.

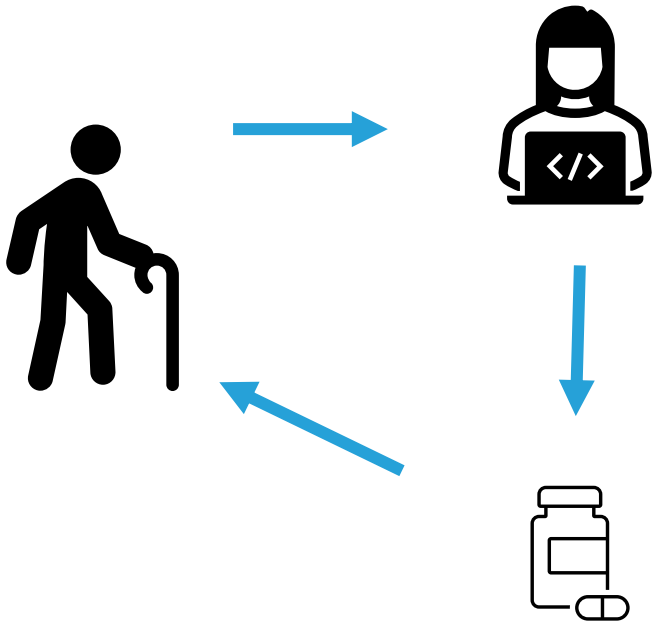
The image below shows how many steps you took on each type of day.

Better than typical Typical Worse than typical

Step count

Better than typical Typical Worse than typical

The vision: remote monitoring of function enables novel and effective methods for Alzheimer’s care and treatment



Thank you

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