Data & Statistical Sciences

Profiling Physical Activities of Patients with Immunological Diseases in Phase 3 Trials

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- The content of this presentation does not communicate results of AbbVie-sponsored Scientific Research.

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Outline

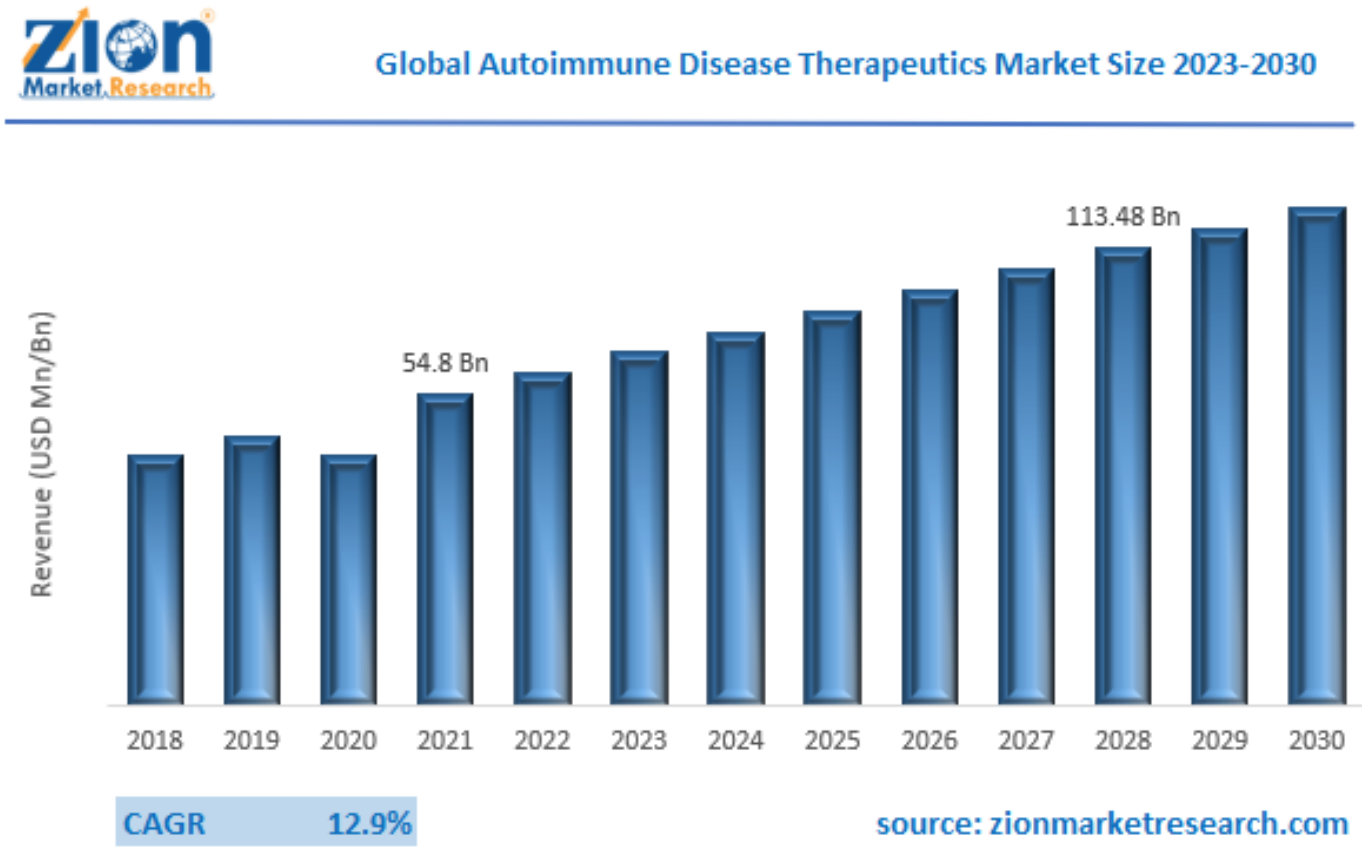
- Why DHT for immunological diseases?
- Our strategy and journey for DHT implementation and value capture
- Physical activities profiles of AxSpa and PPP patients in Ph3 trials
- Summary and outlook

Immunological Diseases Affect A Large Portion of World Population

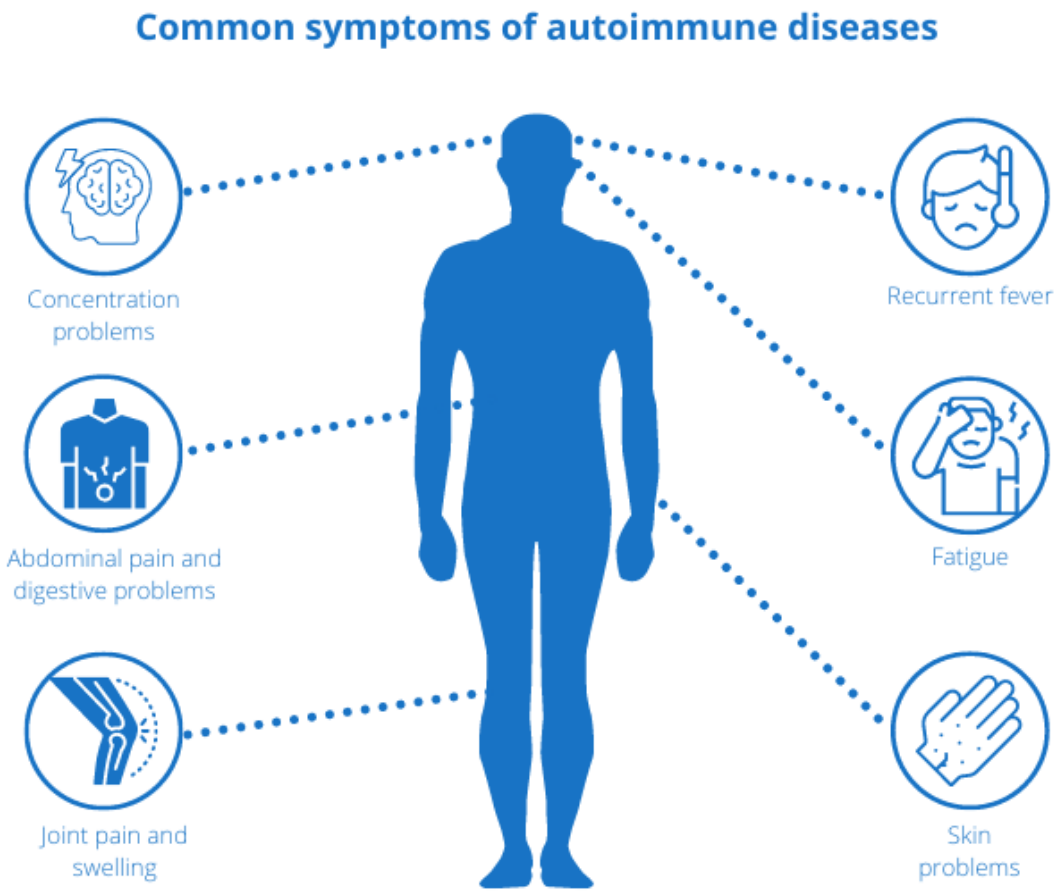
Allergy (30~40%)

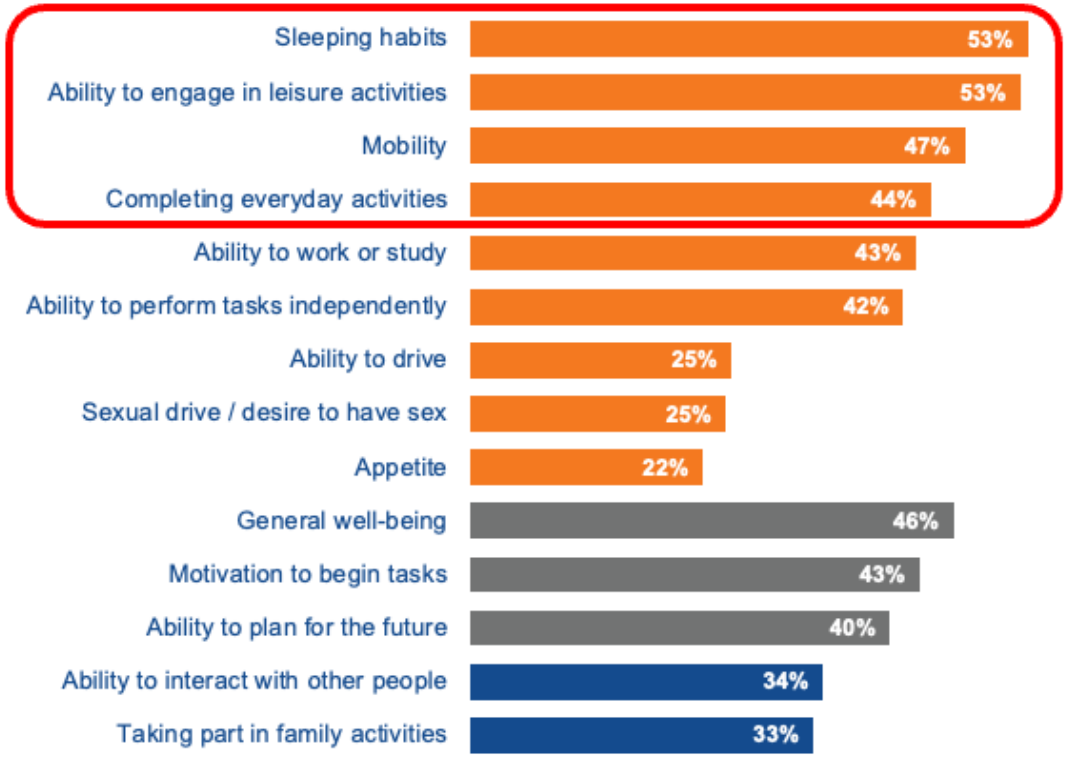
Asthma (8%)

Autoimmune Diseases (10%)



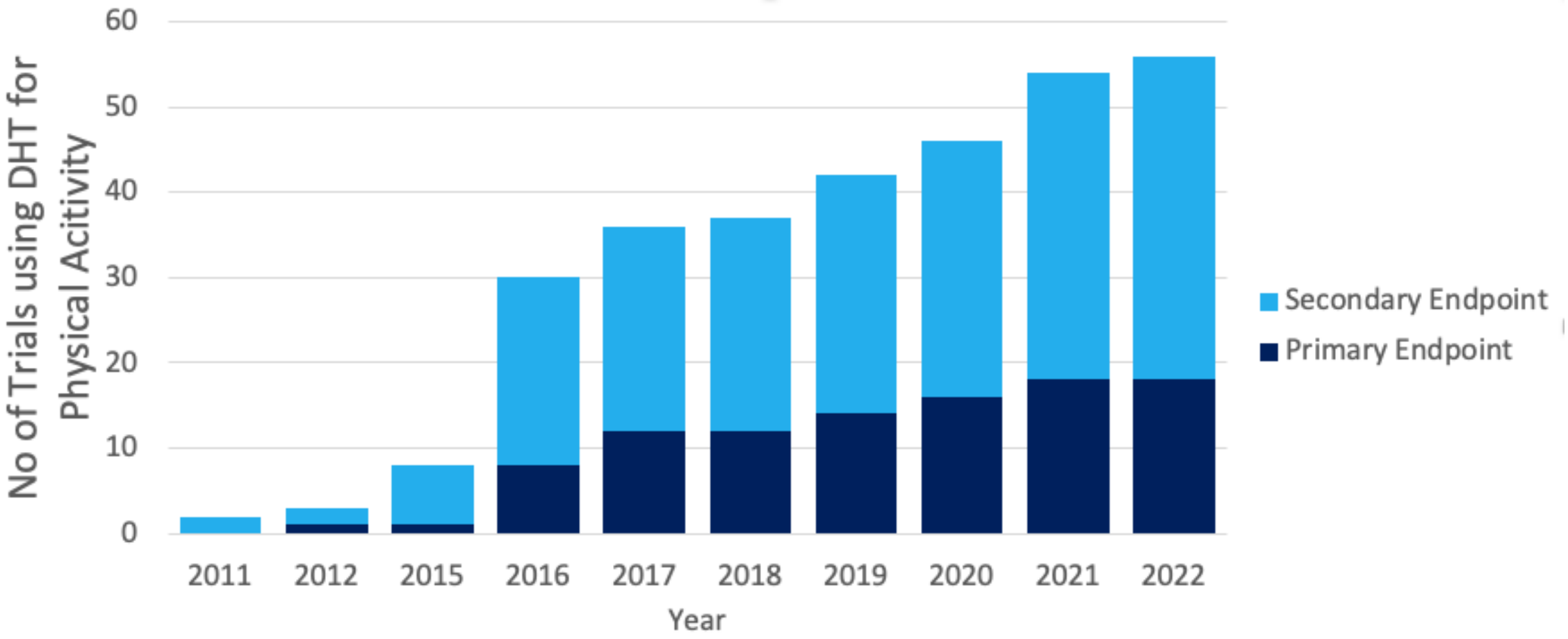
Patients with Immunological Diseases Suffering from Mobility Constrains





Axial Spondyloarthritis (AxSpA) patient survey on impacts of activities in daily life conducted by Research Partnership LivingWith

DHT has been proven to be a fit-for-purpose tool for physical activity profiling with an increased number of clinical trials over time



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DHT has reached the tipping point of harnessing values

The NEW ENGLAND JOURNAL of MEDICINE

Wearable Digital Health Technology

Stephen H. Friend, M.D., Ph.D., Geoffrey S. Ginsburg, M.D., Ph.D., and Rosalind W. Picard, Sc.D.

that wearable DHT is at an inflection point between fanciful descriptions and practical applications that are being woven into health monitoring, clinical diagnoses, and administrative approvals for new therapies. As recently as 5 years ago, almost all discussions about wearable DHT were in the future tense; it is now reasonable to assume that before the end of this decade the use of wearable DHT will be mainstream and underlie many aspects of medical care assessments and decision making for both patients and clinicians.

REVIEW ARTICLE WEARABLE DIGITAL HEALTH TECHNOLOGIES IN MEDICINE

Digital Technology for Diabetes

Michael S. Hughes, M.D., Ananta Addala, D.O., M.P.H., and Bruce Buckingham, M.D.

Metrics

November 30, 2023
N Engl J Med 2023; 389:2076-2086
DOI: 10.1056/NEJMra2215899

REVIEW ARTICLE WEARABLE DIGITAL HEALTH TECHNOLOGIES IN MEDICINE

Wearable Technology in Clinical Practice for Depressive Disorder

Szymon Fedor, Ph.D., Robert Lewis, M.Sc., Paola Pedrelli, Ph.D., David Mischoulon, M.D., Ph.D., Joshua Curtiss, Ph.D., and Rosalind W. Picard, Sc.D.

Figures/Media Metrics

December 28, 2023
N Engl J Med 2023; 389:2457-2466
DOI: 10.1056/NEJMra2215898

REVIEW ARTICLE WEARABLE DIGITAL HEALTH TECHNOLOGIES IN MEDICINE

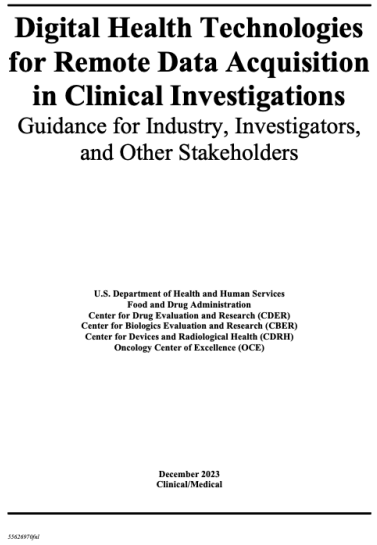
Wearable Digital Health Technologies for Monitoring in Cardiovascular Medicine

Erica S. Spatz, M.D., M.H.S., Geoffrey S. Ginsburg, M.D., Ph.D., John S. Rumsfeld, M.D., Ph.D., and Mintu P. Turakhia, M.D., M.A.S.

cle Figures/Media Metrics

January 25, 2024
N Engl J Med 2024; 390:346-356
DOI: 10.1056/NEJMra2301903

FDA is actively working on the readiness to receive DHT data submission



Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

Guidance for Industry, Investigators, and Other Stakeholders

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Oncology Center of Excellence (OCE)

December 2023
Clinical/Medical

Three focused presentations were given by FDA staff at **Regulatory Education for Industry (REdI) Annual Conference 2023**

PDUFA VI Goals for Digital Health Technologies - A Regulatory Review Perspective.pdf	**Andrew Potter** *Mathematical Statistician* Division of Biometrics I (DBI) Office of Biostatistics (OB) Office of Translational Sciences (OTS) | CDER
PDUFA VII Goals for Digital Health Technologies (DHT) - An IT Perspective.pdf	**Mary Ann Slack** *Director* OSP | CDER
The Modernization of Clinical Trials through Digital Health Technologies (DHT), Decentralized Clinical Trials (DCT) and Point of Care Trials.pdf	**Beth Kunkoski** *Health Science Policy Analyst* Clinical Methodologies Office of Medical Policy (OMP) | CDER

AbbVie Digital Science team uses DHTs to modernize outcome measurements and accelerate drug development

TA Digital Strategy

- Partner with IEST/AST members to develop proper **Concept of Interests** (i.e., Digital Biomarkers and/or Novel Outcome Measures) with **clinical, patient and regulatory alignment**
- Design NDE development and validation strategy following V3 framework and regulations
- Also partner with **medical affairs** and **commercial** for post-marketing strategies

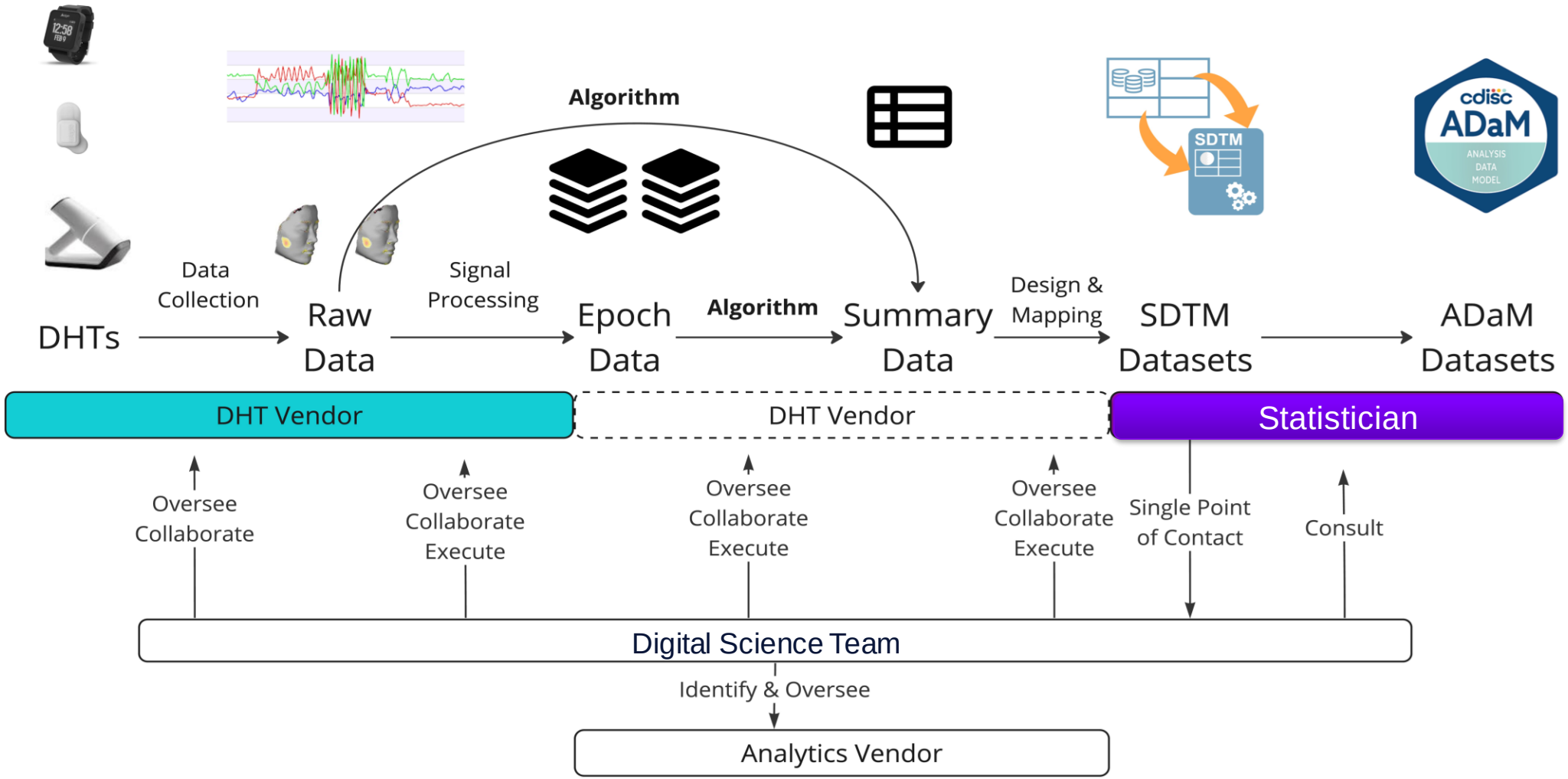
DHT Search & Evaluation

- Identify **best-in-class** and clinically **fit-for-purpose DHTs** for biomarkers and outcome measures
- Develop and maintain DHT library and manage vendors relationships
- Partner with CSG on DHT partnerships S&E

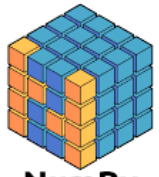
Digital Data Analytics and Digital Science Lab

- Conduct **DHT verification** and **usability testing**
- **Algorithms** development and validations
- Responsible for DHT signal processing and Digital data analyses for **AbbVie portfolio**
- Establish regulatory-compliant Digital Data Analytics **Capabilities**

Digital Science Team fills the gaps in DHT data operation in clinical trials



AbbVie internal digital data toolkit (DDTK) was developed to automate the data process



NumPy

pandas

plotly

AbbVie Digital Health Data Toolkit (DDTK)

This repo is for the development of digital data analytics toolkit. It will process patient-level clinical outcomes and continuous digital device data. The key components include sensor (accelerometer and gyroscope) data pre-processing (denoising, resampling, gravity removal/adjustment), segmentation, feature calculation, data visualization, and modeling.

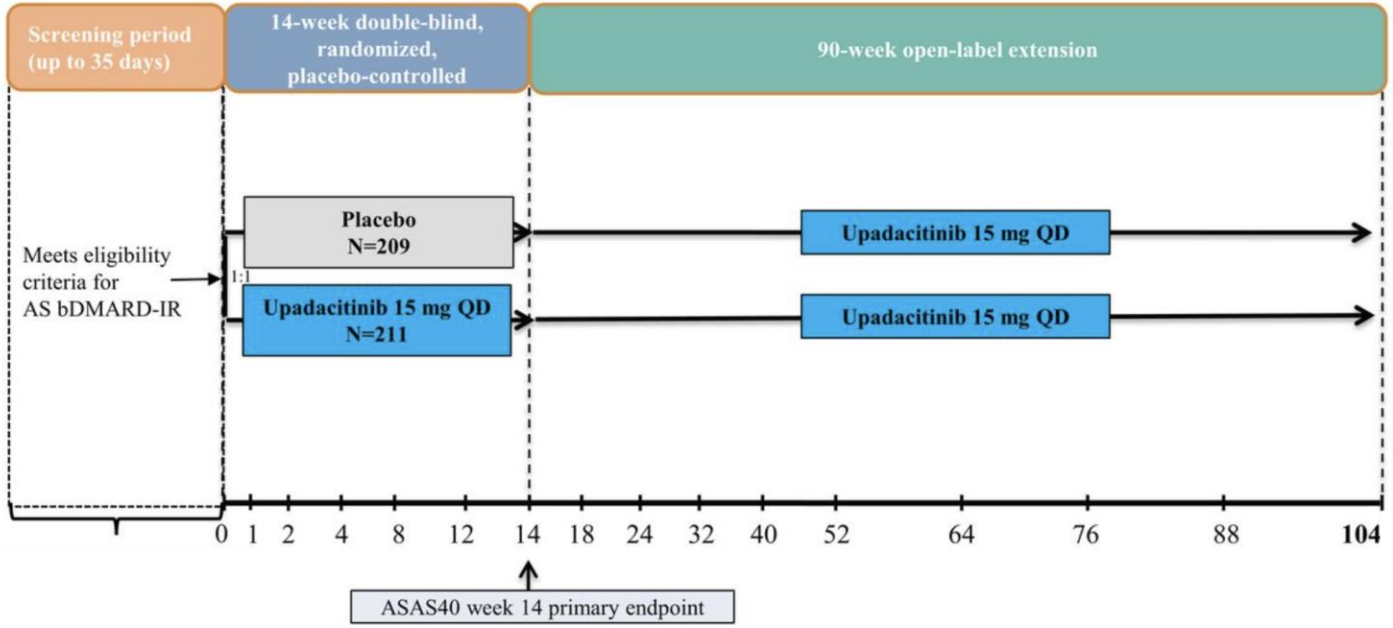
Repo Structure

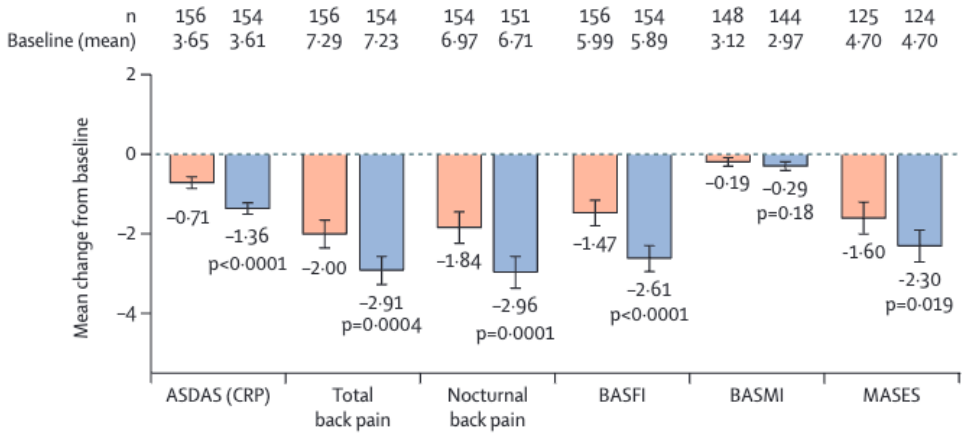
```
ddtk
├── LICENSE
├── README.md
├── digitalProcessor.py
├── digiPlot.py
├── requirements.txt
├── utils.py
├── processor
│   ├── models
│   ├── actigraph
│   ├── apdm
│   ├── empatica
│   ├── pkg
│   ├── __init__.py
│   ├── models.py
│   ├── sites.py
│   ├── patients.py
│   └── studies.py
├── data
│   ├── __init__.py
│   ├── dataproc.py
```

- **Key Features:**
  - Study data ETL
  - Sensor signal processing
  - Feature engineering
  - Algorithm development
  - Data Visualization

Data scientists and statisticians can easily pull the data using a few lines of commands in the Jupyter Notebook

SELECT-AXIS 2 is a Phase 3 study to investigate the efficacy and safety of Upadacitinib in patients with ankylosing spondylitis





14 weeks of continuous actigraphy monitoring in PBO and UPA arms for exploratory purposes

- Physical Activities
- Sleep
- Spinal Range of Motion
- Morning Stiffness

Actigraph CentrePoint Insight Watch

A. Deodhar *et al.*, *Lancet*. **400**, 369–379 (2022).

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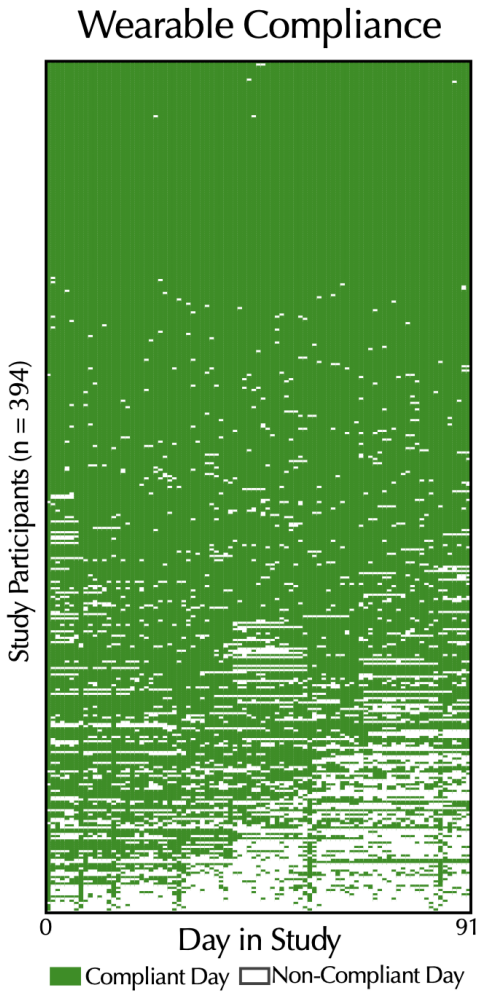
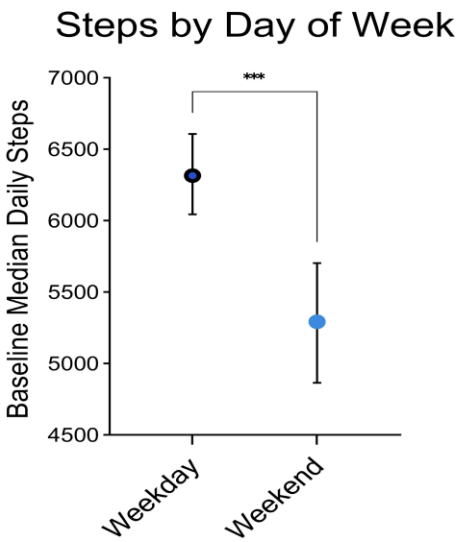
The study demonstrated a high compliance and retention rate

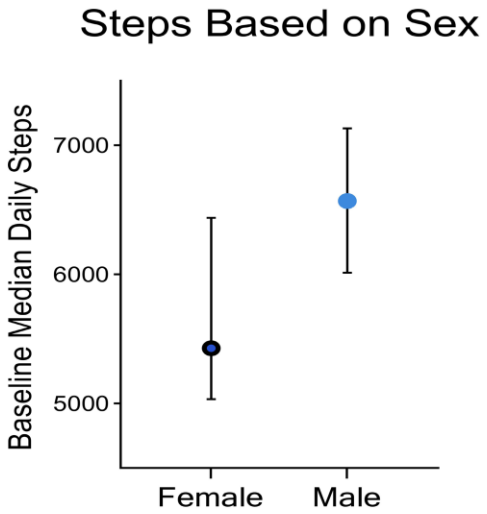


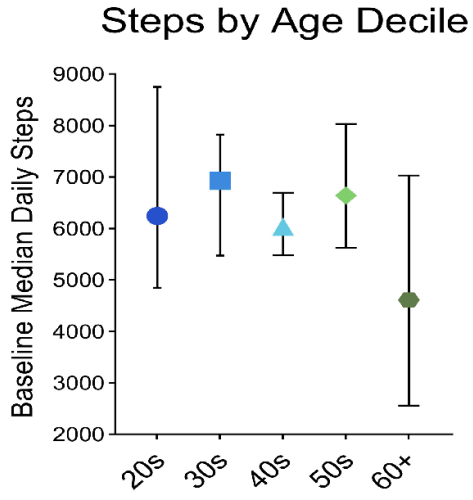
- Of 420 total patients, physical activity data was collected from 394 participants, and 312 patients met minimal adherence criteria at baseline (i.e., the first week)
  - Compliance is defined as wearing 16 hours per day
- Through 14 weeks, adherence was demonstrated for 83.5% of study days, excluding clinical visit days
  - Participants did not wear during the clinical visit

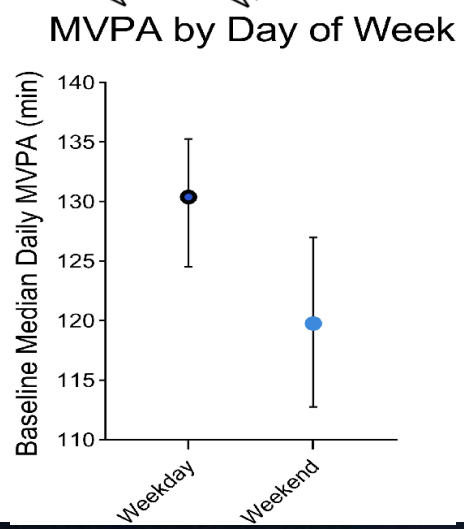
Mease PJ et. al., EULAR, 2022

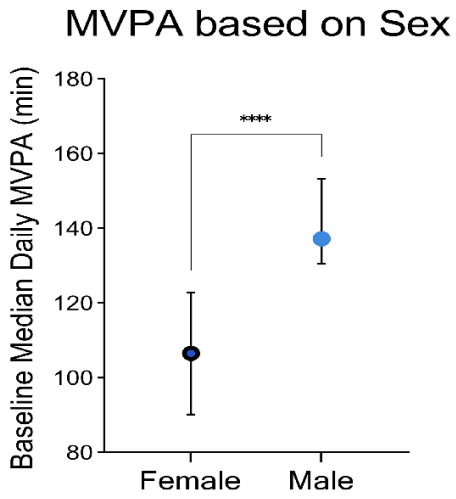
Daily step counts and MVPA are used as physical activity surrogate

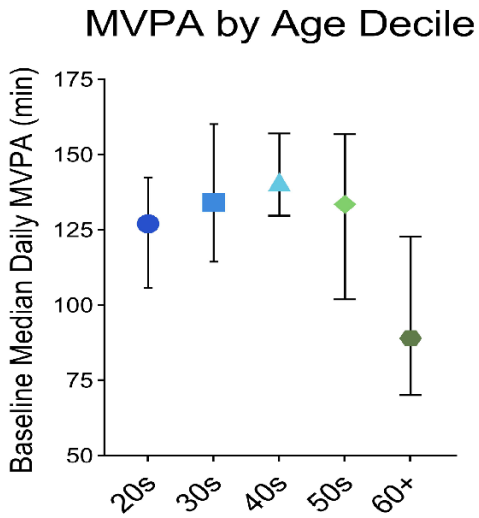












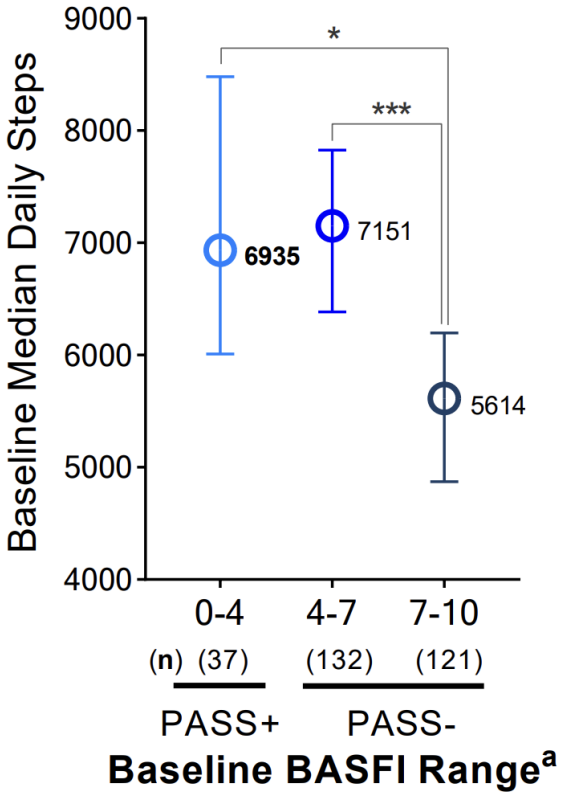
Physical Activity at Baseline

- Weekdays > Weekends
- Male > Female
- Age difference

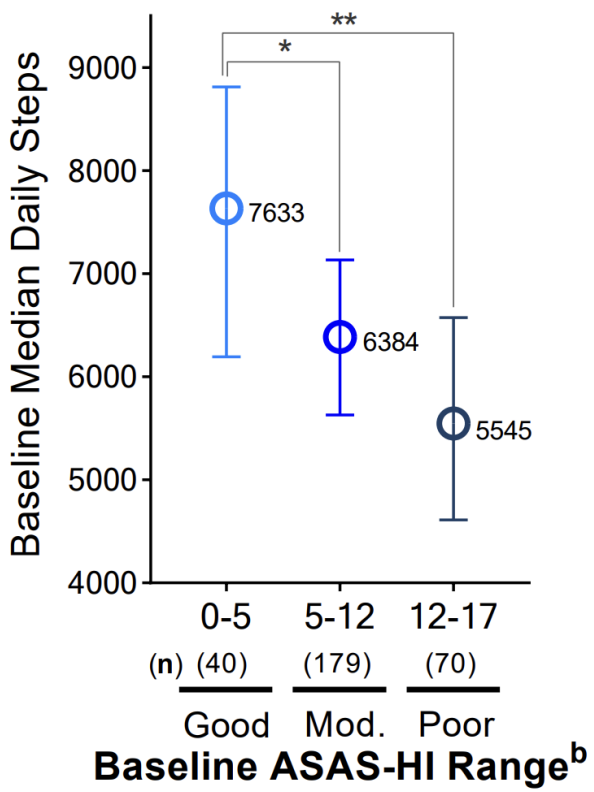
Mease PJ et. al., EULAR, 2022

Baseline physical activity measured by step counts aligns with patient self-reported disease severities

Steps by Functional Index



Steps by Health Status



BASFI: Bath Ankylosing Spondylitis Functional Index

9) Doing physically demanding activities (e.g physiotherapy exercises, gardening or sports).

Easy ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10 Impossible

10) Doing a full days activities whether it be at home or at work.

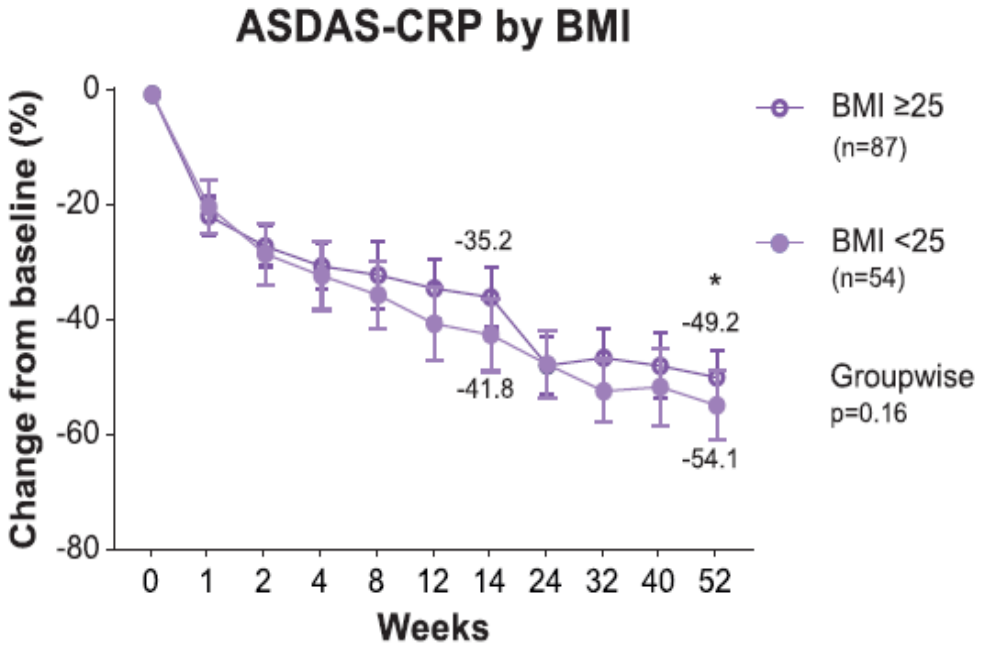
Easy ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10 Impossible

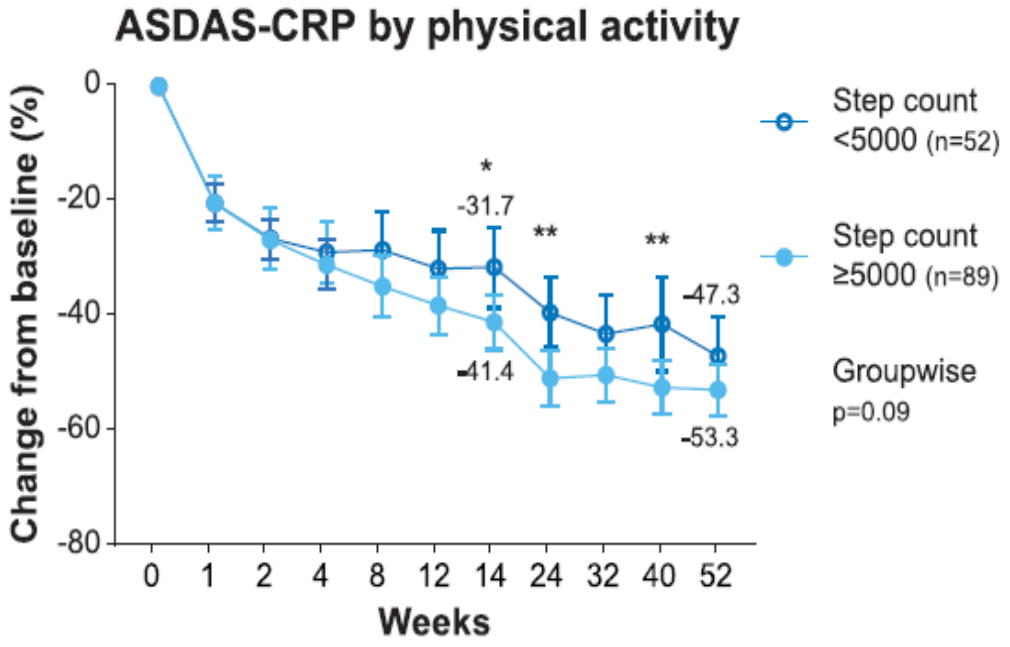
ASAS-HI: Assessment of Spondyloarthritis International Society Health Index

1. Pain sometimes disrupts my normal activities.
   - ☐ I agree
   - ☐ I do not agree
2. I find it hard to stand for long.
   - ☐ I agree
   - ☐ I do not agree
3. I have problems running.
   - ☐ I agree
   - ☐ I do not agree

Mease PJ et. al., EULAR, 2022

Baseline step counts is suggested to be a better predictor of outcome than BMI



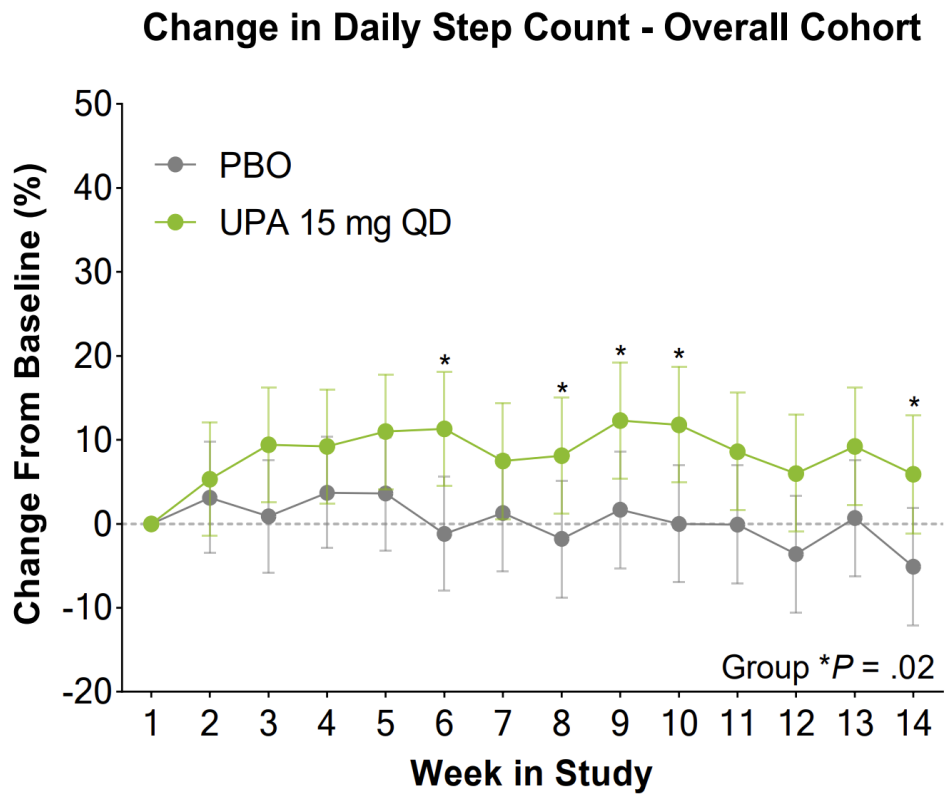


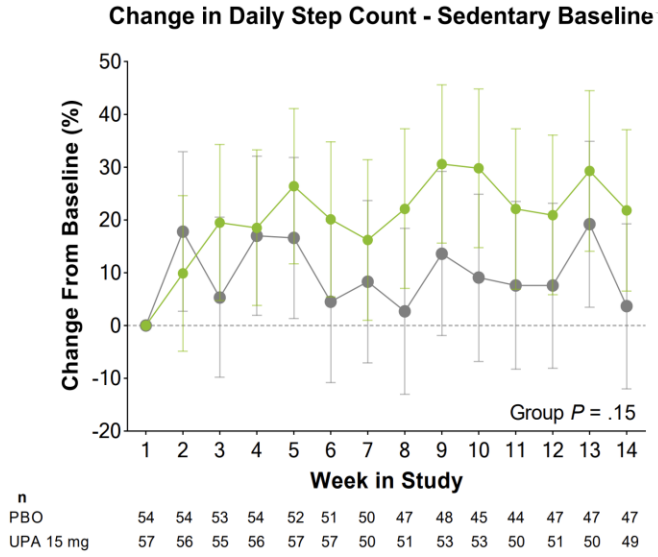
Change From Baseline in ASDAS(CRP) in Patients Receiving Upadacitinib 15 mg QD Stratified by Baseline BMI or Physical Activity Levels

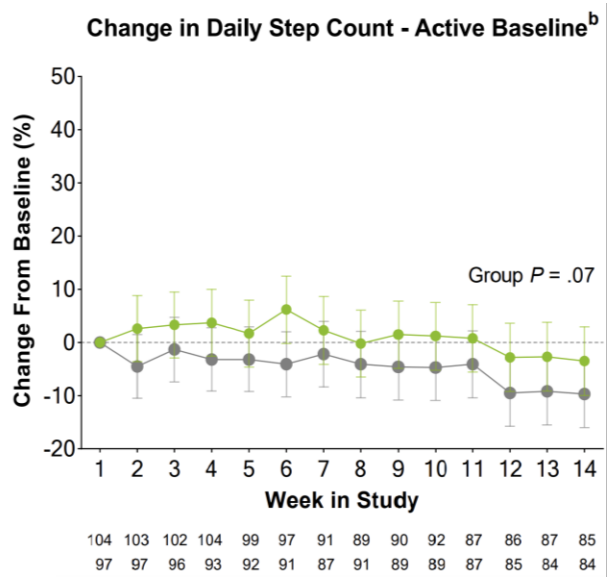
- ASDAS is a composite index that assesses disease activity
- Step counts < 5000 is considered as sedentary
- Physical activity measured by step counts demonstrated a trend towards greater reduction in ASDAS(CRP) at most time points from week 8 onwards

Crowley A et. al., ACR Abstract, 2023

Treatment of Upadacitinib is associated with increased physical activity measured by daily step counts







Increased physical activity with upadacitinib vs. placebo in the cohort overall, with a more pronounced effect in the sedentary population, suggesting a possible 'ceiling effect'*

Curtis JR et. al., ACR Abstract, 2023

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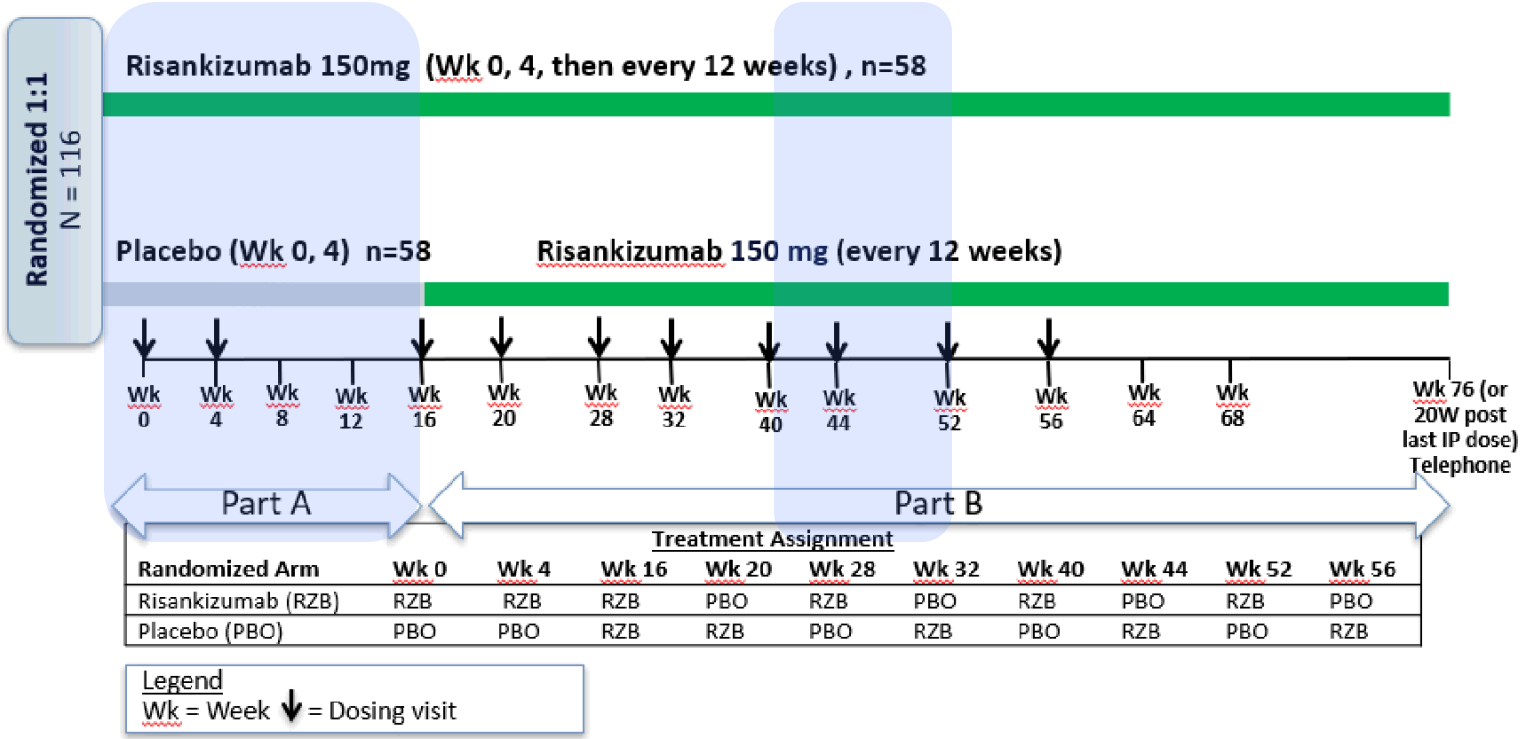
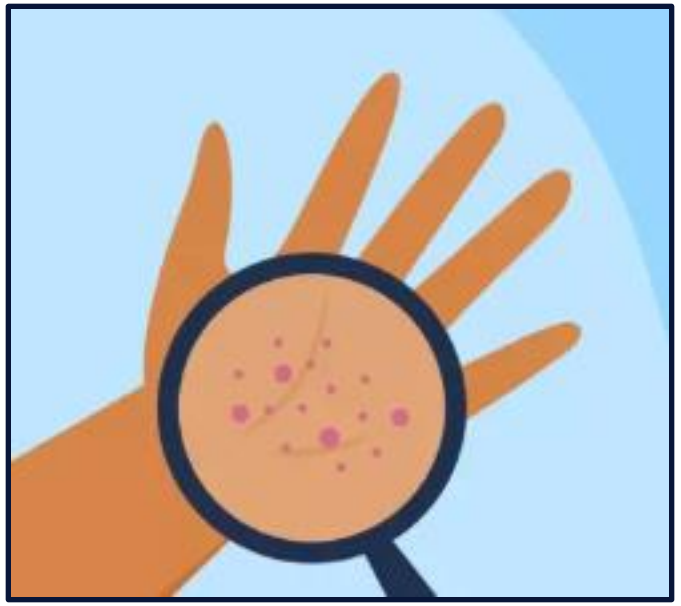
JumPPP is a phase 3 study investigating the effect of Risankizumab in Japanese patients with Moderate-to-Severe Palmoplantar Pustulosis



Randomized Arm	Wk 0	Wk 4	Wk 16	Wk 20	Wk 28	Wk 32	Wk 40	Wk 44	Wk 52	Wk 56
Risankizumab (RZB)	RZB	RZB	RZB	PBO	RZB	PBO	RZB	PBO	RZB	PBO
Placebo (PBO)	PBO	PBO	RZB	RZB	PBO	RZB	PBO	RZB	PBO	RZB

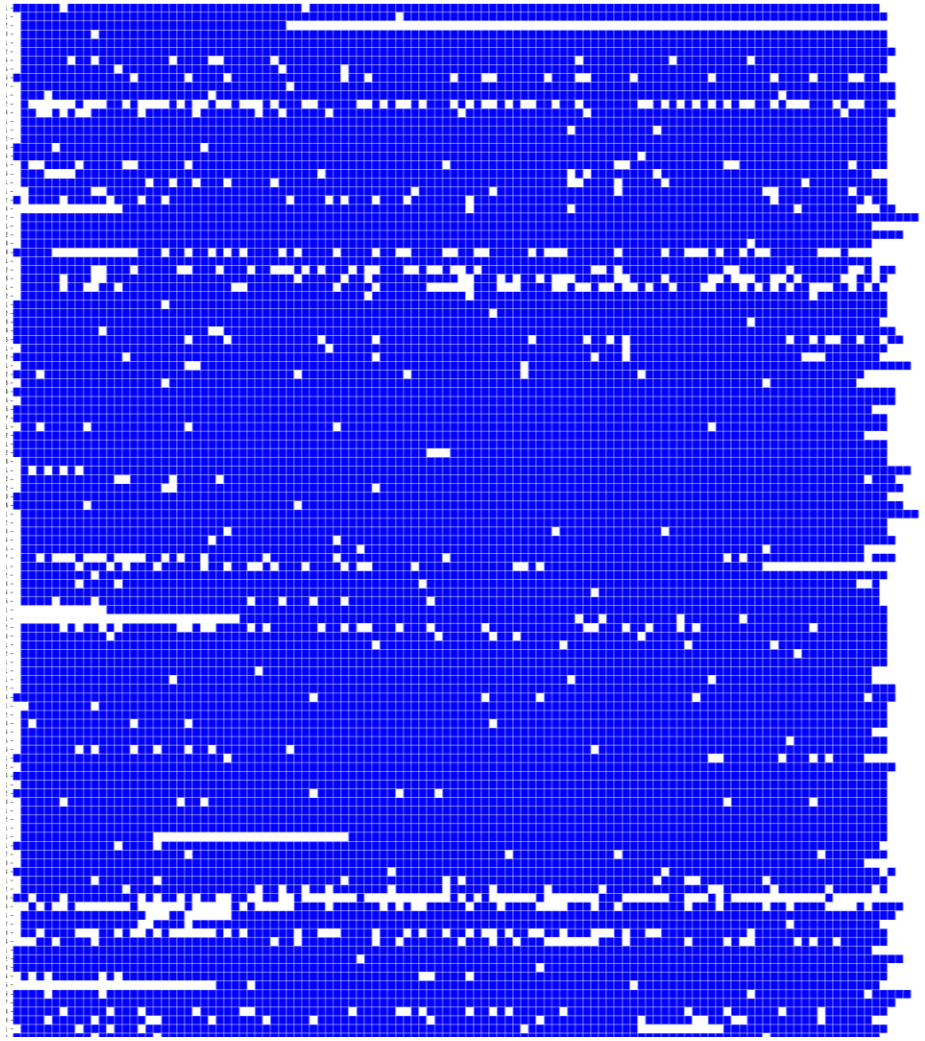
PBO = placebo; RZB = risankizumab; Wk = week



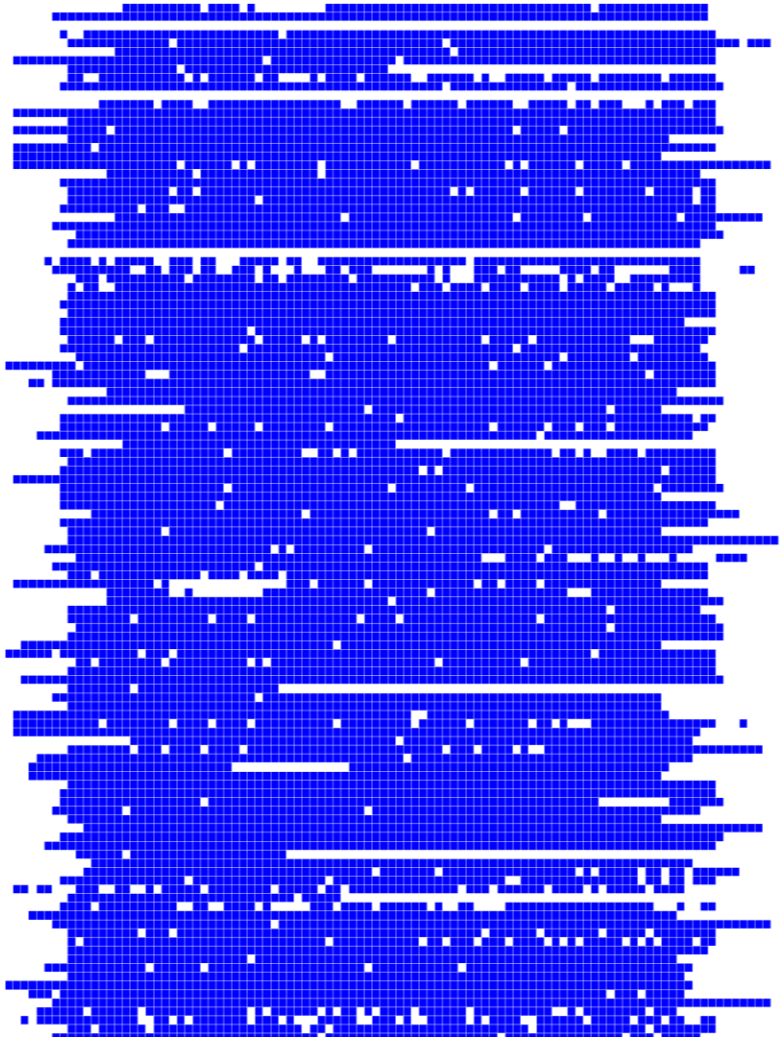
- **Sterile pustules**
- **Thick plaques (psoriasis)**
- **Itching**
- **Pain or a burning sensation**
- **Fissuring (Cracked skin)**

Continuous physical activity monitoring during day time using Actigraph CentrePoint Insight Watch from baseline to Wk16 and Wk40 to Wk52

The study demonstrated a high compliance and retention rate

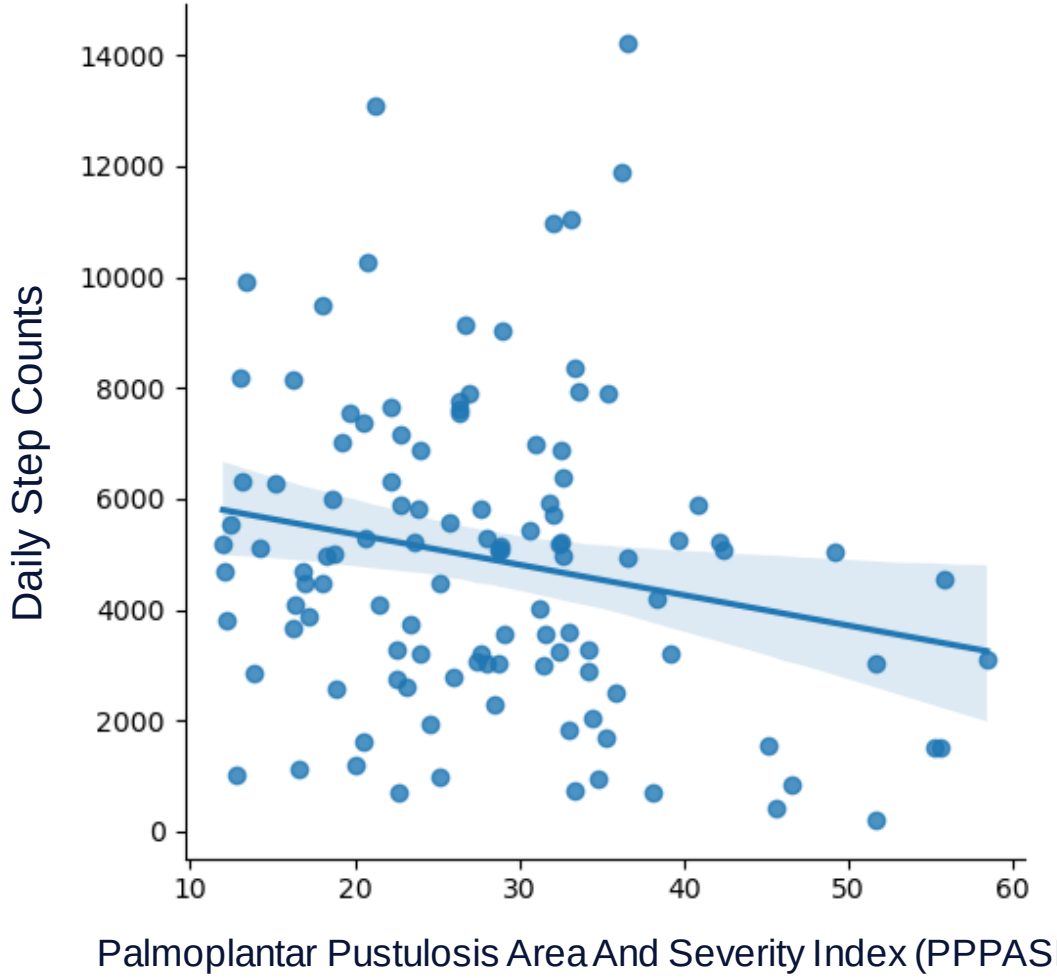


- Compliance (12h wearing):
  - Period A: 89.8%
  - Period B: 83.3%
- On weekly (>3 day) basis:
  - Period A: 97%
  - Period B: 95%



Study Day

Physical activity measured by step counts showed a moderate association with disease status at baseline



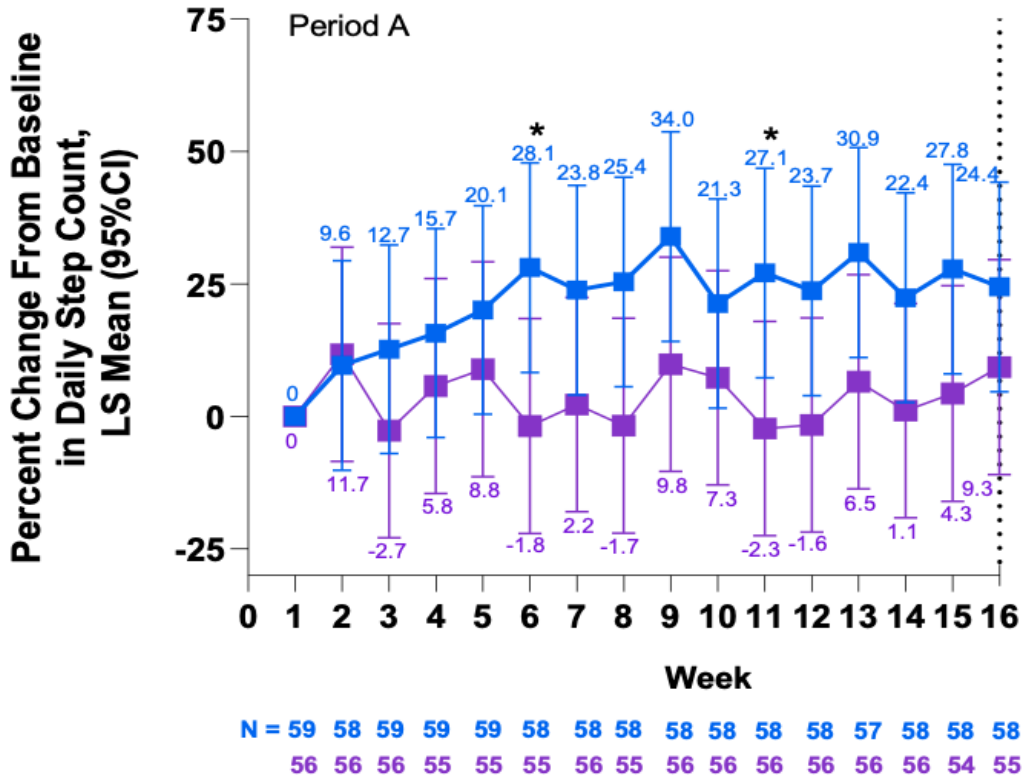
OLS Regression Results

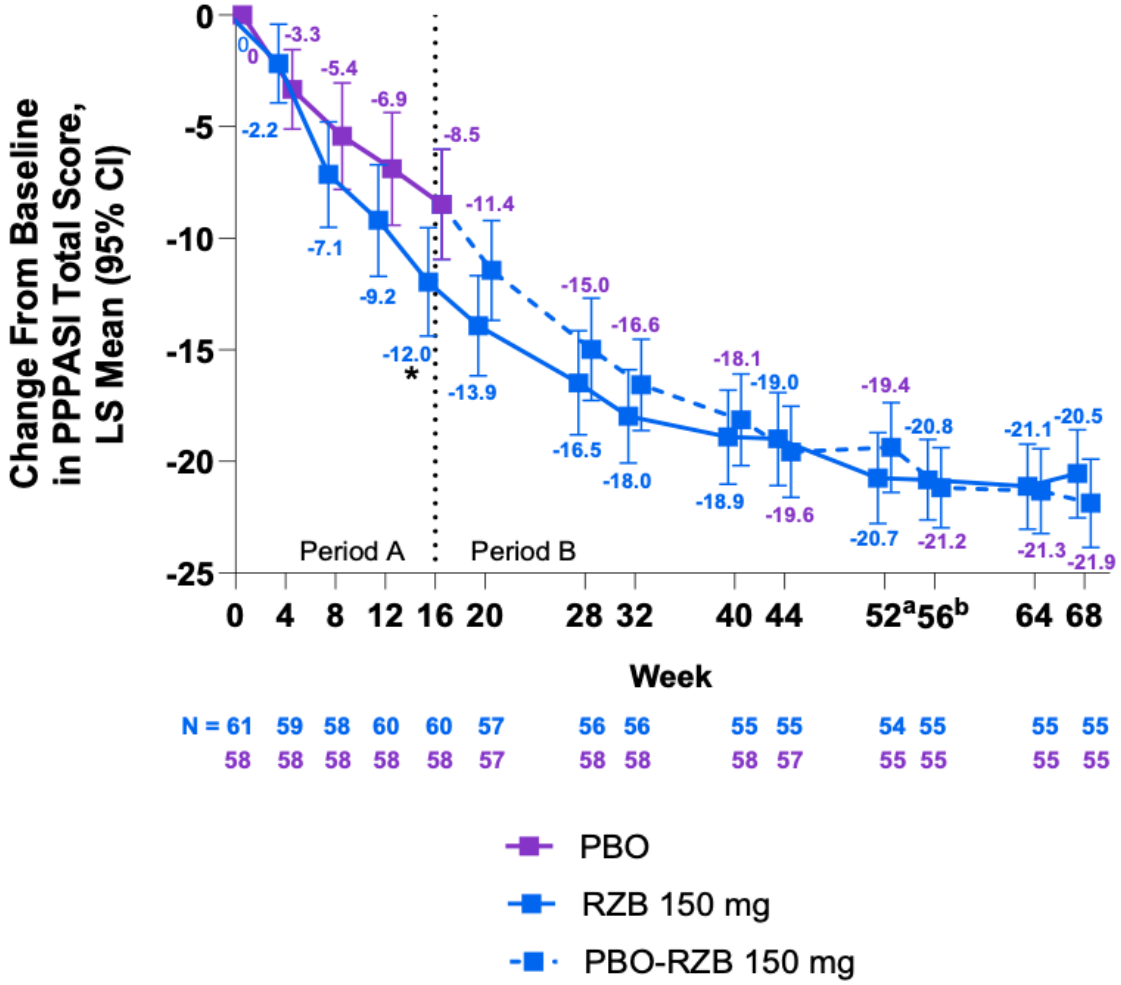
Dep. Variable:	wearFilteredSteps	R-squared:	0.042
Model:	OLS	Adj. R-squared:	0.034
Method:	Least Squares	F-statistic:	4.987
Date:	Fri, 26 Jan 2024	Prob (F-statistic):	0.0275
Time:	04:55:54	Log-Likelihood:	-1072.6
No. Observations:	115	AIC:	2149.
Df Residuals:	113	BIC:	2155.
Df Model:	1		
Covariance Type:	nonrobust		

	coef	std err	t	P>|t|	[0.025	0.975]
Intercept	6459.4276	740.248	8.726	0.000	4992.864	7925.991
PPPASIBL	-54.8856	24.577	-2.233	0.028	-103.576	-6.195

Omnibus:	16.710	Durbin-Watson:	2.091
Prob(Omnibus):	0.000	Jarque-Bera (JB):	19.559
Skew:	0.859	Prob(JB):	5.66e-05
Kurtosis:	4.062	Cond. No.	87.2

Physical activity measured by step counts demonstrated treatment effect as early as week 6





Lessons learned

- “Fit-for-purpose” DHT and measurements are critical to harnessing the value
- Baseline data collection needs to be designed into the study operation
- Innovative analytical methodologies may generate further insight into the continuous physical activity data
- Further validation of the physical activity algorithm in the specific patient group should be conducted per FDA guidance

Thank you