From Snapshots to Dynamics:
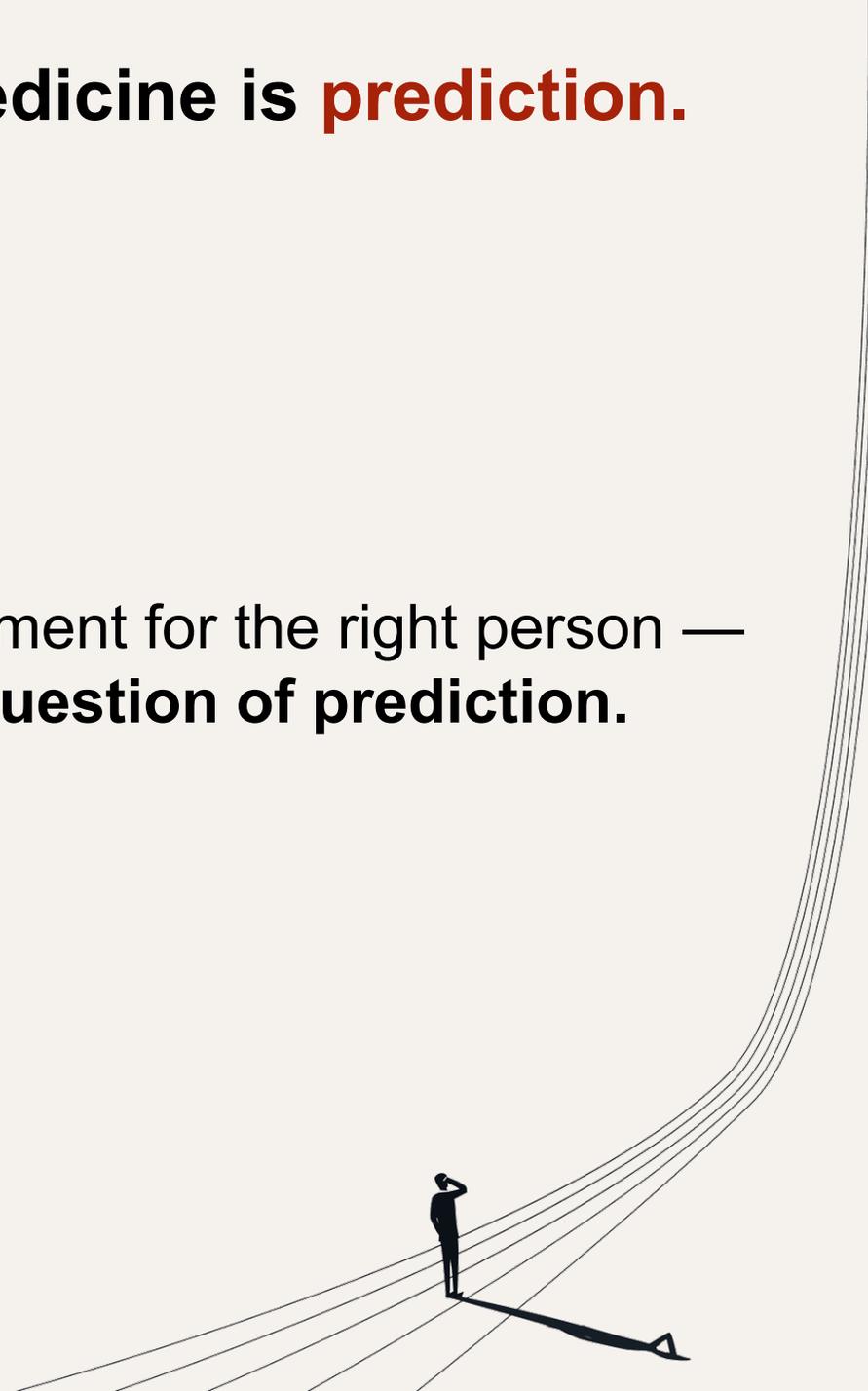# Rethinking Prediction in Precision Psychiatry

Dr. Frederike Petzschner
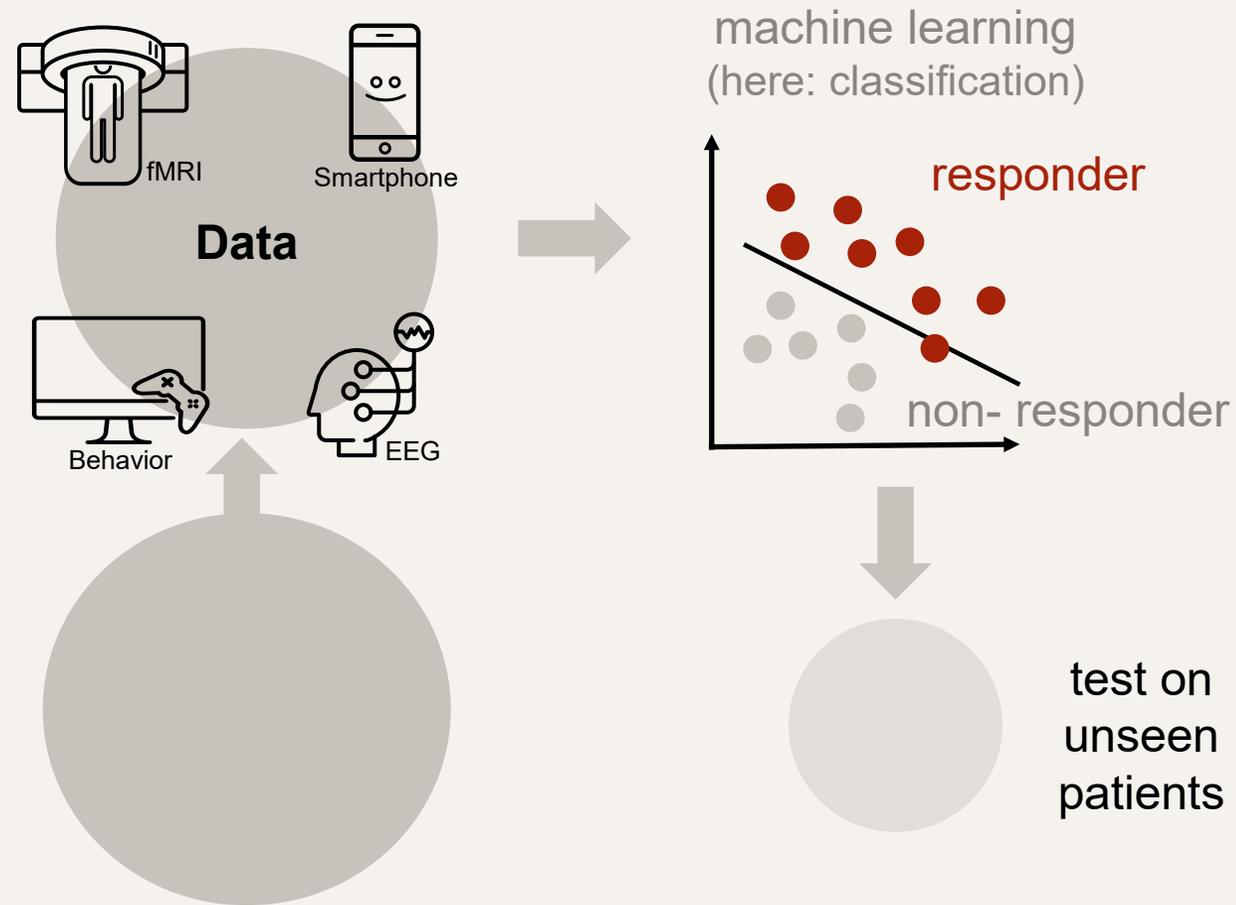Website: fpetzschner.com/lab
Mail: frederike_petzschner@brown.edu

The holy grail of precision medicine is prediction.

Finding the right treatment for the right person —
is fundamentally a question of prediction.

The promise of machine learning.

Sift through heterogeneous data at scale —
and let the algorithm predict who will get better.

*Gordon, Kafui, **Petzschner,** Cell, 2024*

But. Models *fail* to generalize – especially in psychiatry.

Predicting treatment response to antipsychotic medication
for schizophrenia in five independent clinical trials.

Predictions are well above
chance within a single trial...

…but do not generalize across trials.
They fail to predict unseen patients.

FE = first episode
outcome: PANSS change

Science

MEDICINE

Practical challenges for precision medicine

The prediction of individual treatment responses
with machine learning faces hurdles

By **Frederike H. Petzschner**

have the capacity to analyze large datasets

Chekroud et al., **Science***, 2024; Petzschner,* **Science,** *2024*

The *Input* Problem: The data we collect doesn't reflect the disorder

In psychiatry especially — we need to measure the brain in critical moments, not at rest

~~Big Data?~~
Deep Data!

**What we collect:** Questionnaires, sparse assessments — *very little that carries information about mechanisms.*

We measure descriptions.
Not *mechanisms.*

- **Targeted cognitive paradigms** — learning, decision-making under uncertainty
- **Symptom-provoking assessments** — engage the symptom
- **Computational Psychiatry** — model underlying computation in the brain

*Huys et al., **Nature Neuroscience**, 2016; Stephan et al., **Neuron**, 2015; Brodersen et al., **PLoS CB**, 2011; Wiecki et al., **PLoS ONE**, 2016; Wiecki et al., **Clinical Psychological Science**, 2015*

The *Output* Problem: We measure a moment, not a trajectory.

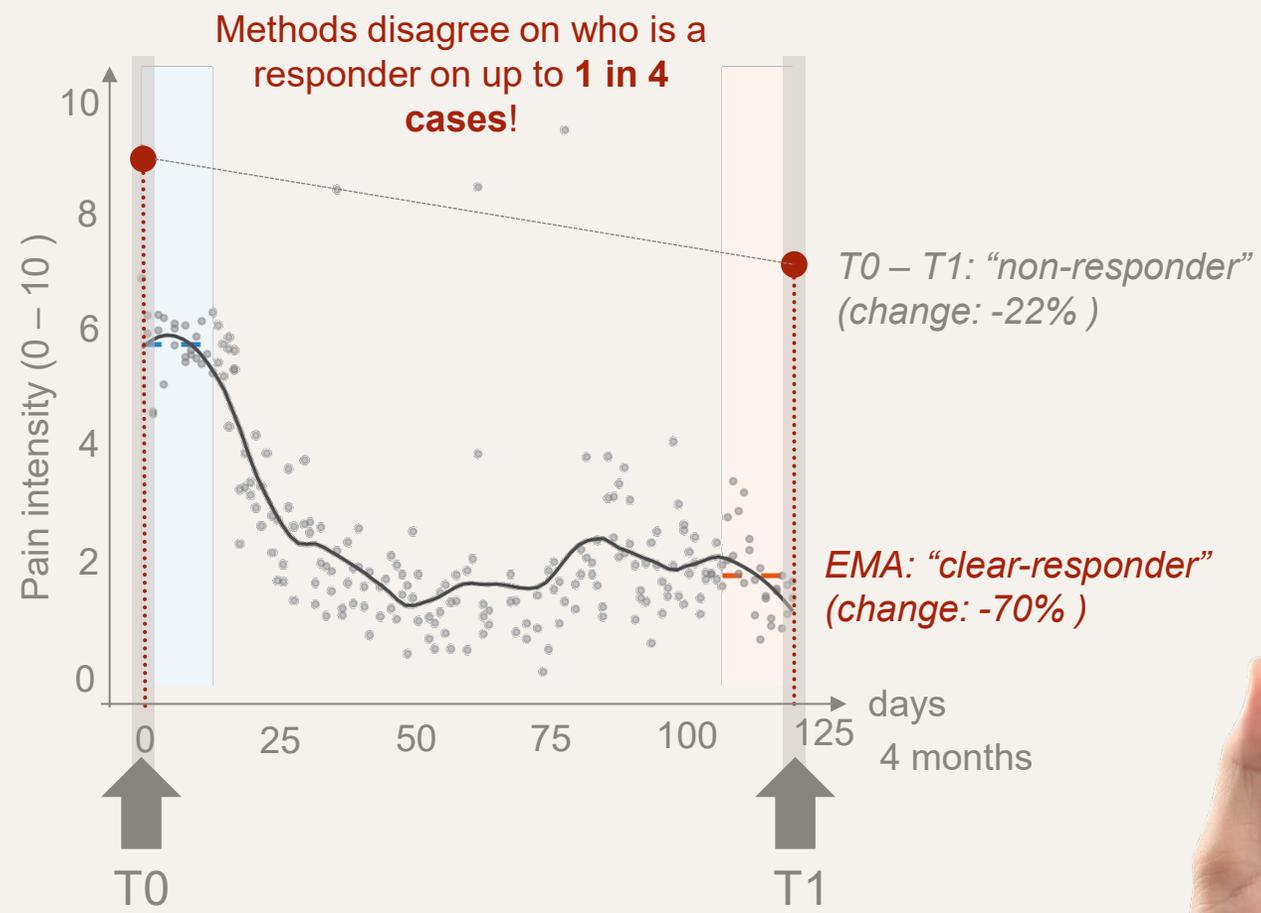Example Pain: One of the most common outcome measures in clinical trials

time

T0

T1
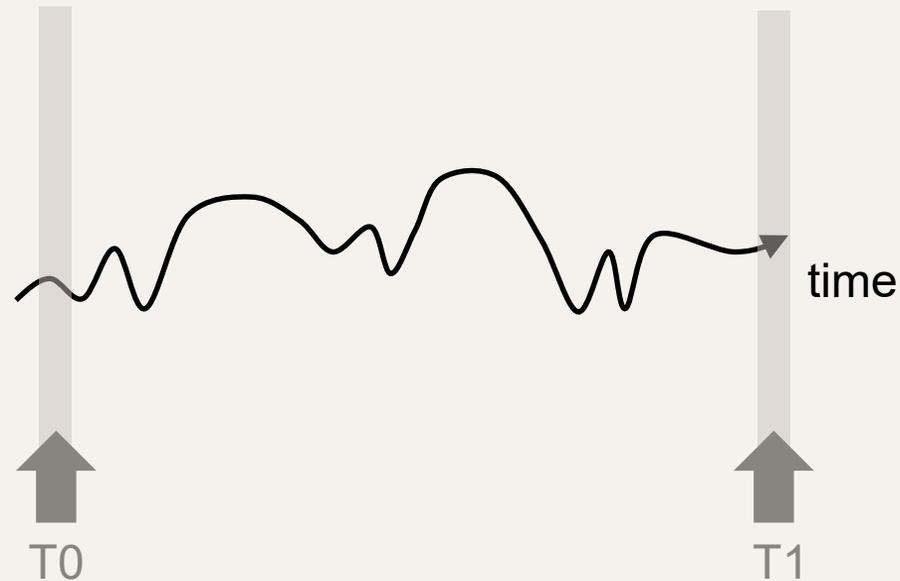
Standard clinical trial measure:
Single time-point report:
"*average pain over the past week*"

Responder defined as:
3-point change, or 30 or 50%
reduction in pain

# The *Output* Problem: We measure a moment, not a trajectory.

Example Pain: Single-point pain assessments lead to false outcomes

Methods disagree on who is a responder on up to **1 in 4 cases**!

T0 – T1: "non-responder" (change: -22%)

*EMA: "clear-responder"* (change: -70%)

n = 219
data points: 50000

Most people will "respond" just by chance.

Draw any two random pain ratings from the same person —
and the majority look clinically significant.

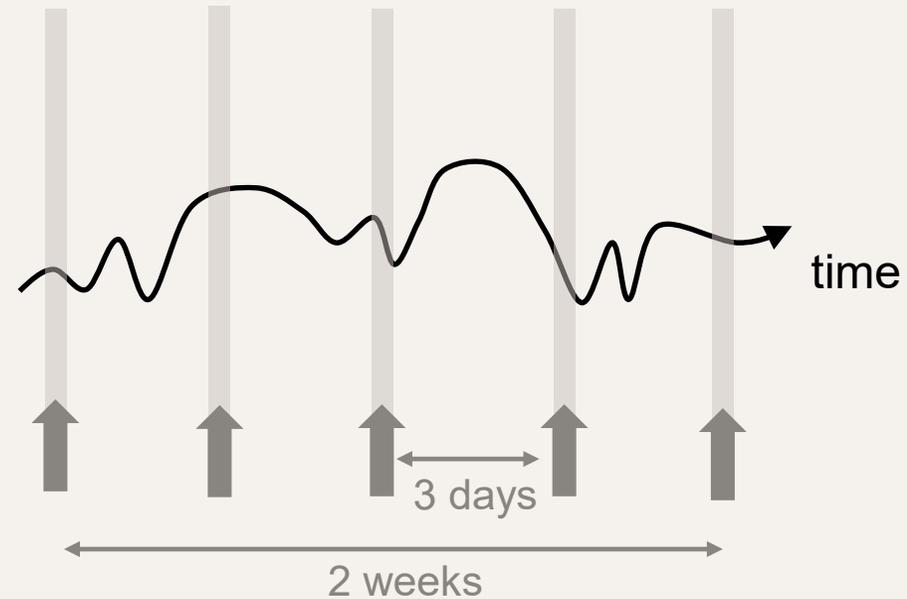*Gunsilius, Heffner, Petzschner, **in prep***
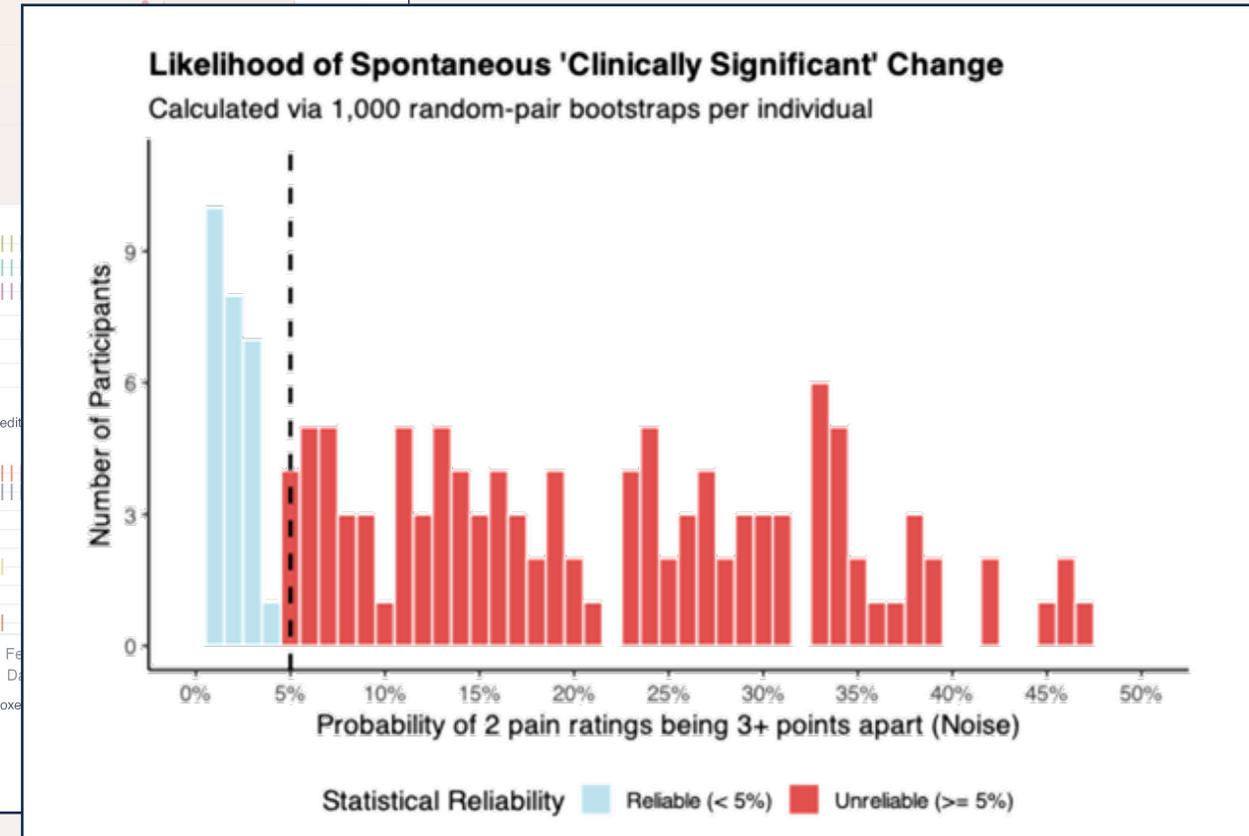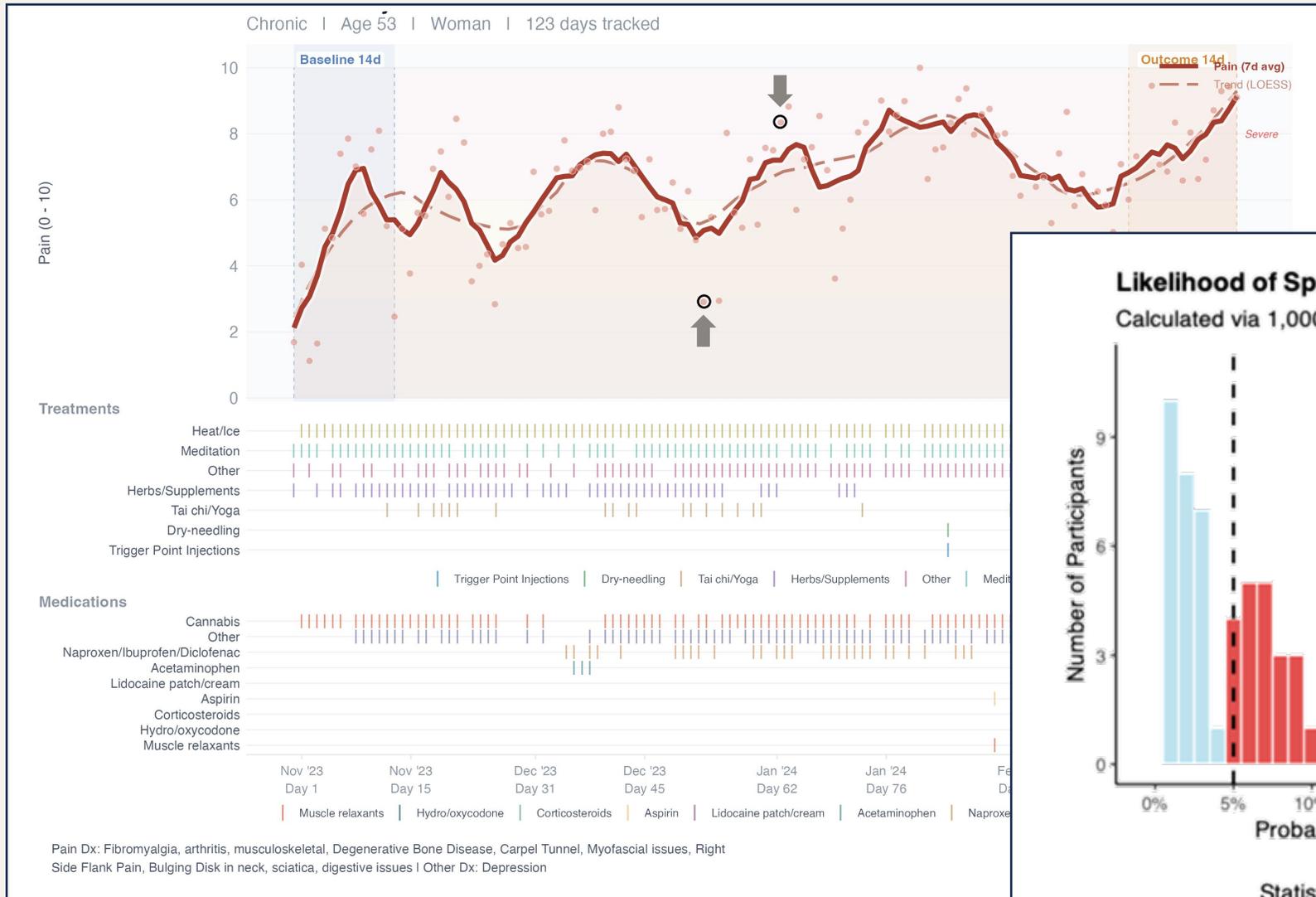
We need longitudinal (wide) data. But not as much as you think.

Pain correlates strongly day-to-day — but that correlation collapses after 3 days. Five measurements spaced across two weeks captures the full picture (κ = 0.65–1.00; ≤3.2% discordance).
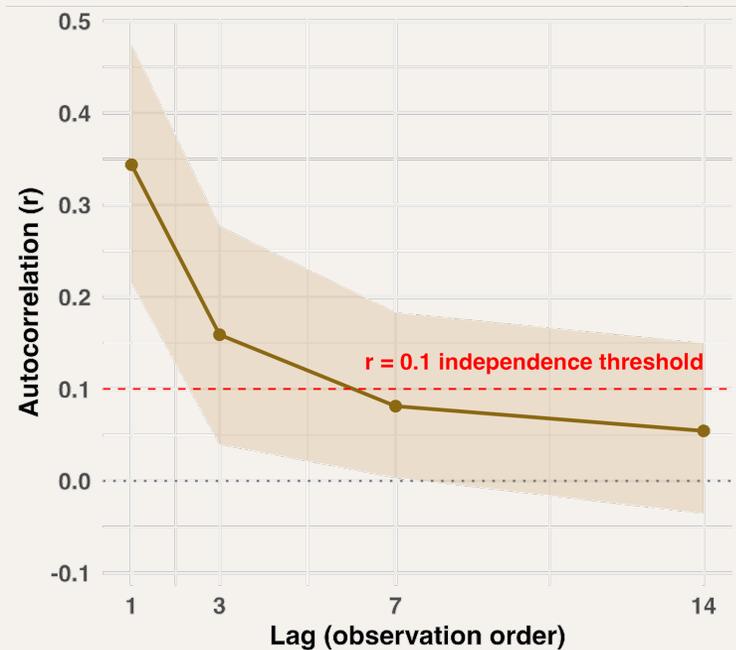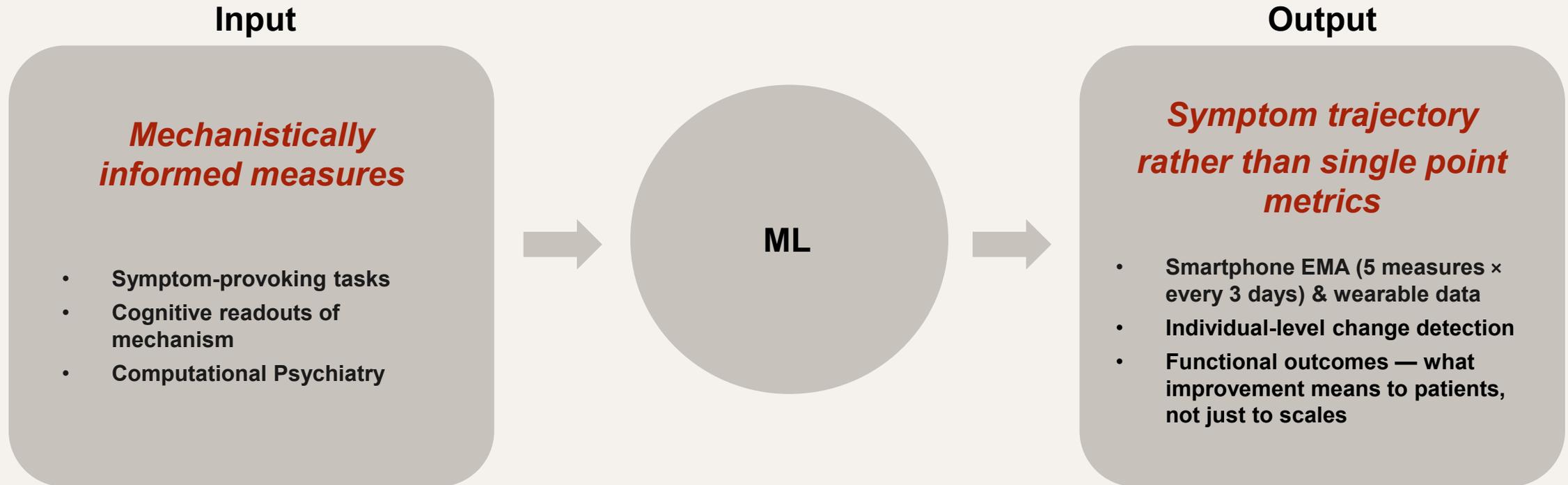

5 total measures x every three days

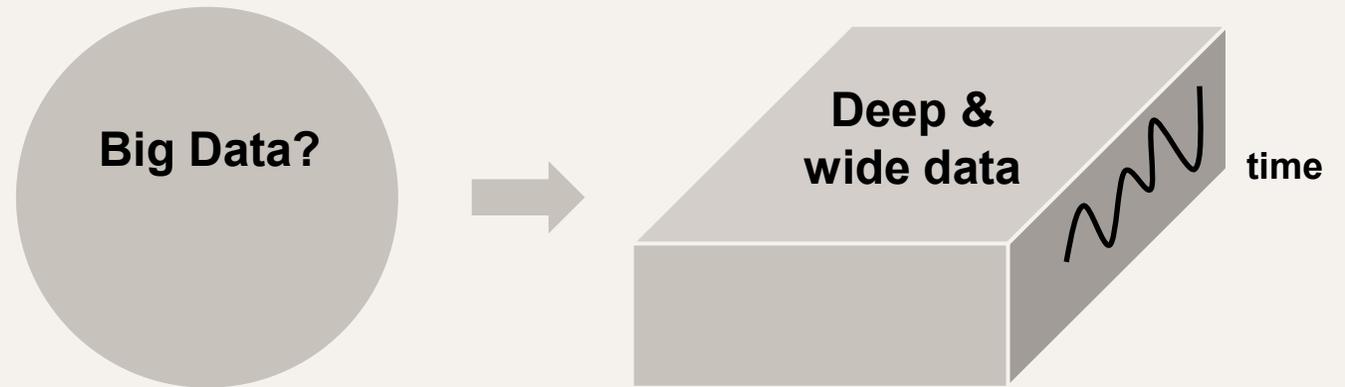This is achievable with a smartphone app. The barrier isn't technological.

Gunsilius, Heffner, Petzschner, in prep

Precision medicine doesn't have a machine learning problem.
It has a *measurement* problem.

Input

Output

Mechanistically informed measures

- Symptom-provoking tasks
- Cognitive readouts of mechanism
- Computational Psychiatry

ML

Symptom trajectory rather than single point metrics

- Smartphone EMA (5 measures × every 3 days) & wearable data
- Individual-level change detection
- Functional outcomes — what improvement means to patients, not just to scales

Precision medicine won't be won with more data on *less informative* variables.

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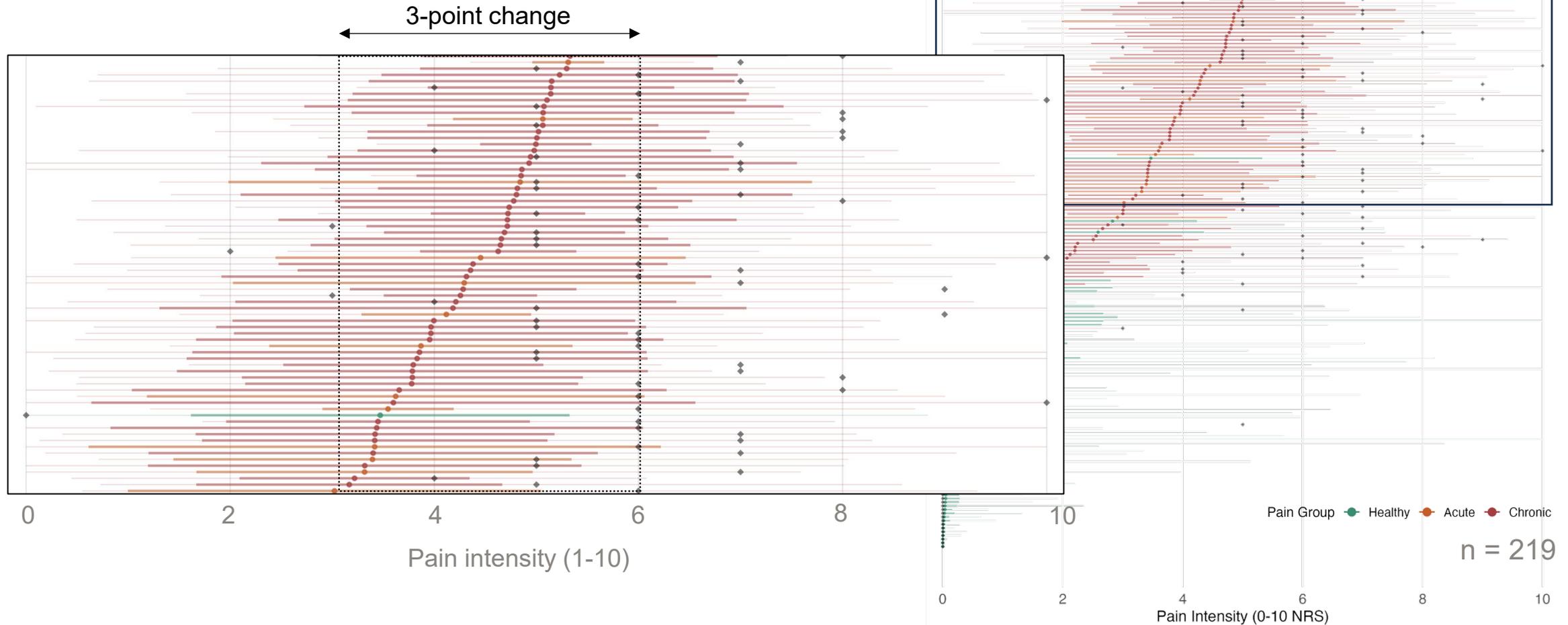**Chris Moore** (Brown)
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A 3-point pain change is not a treatment signal — it's natural fluctuation.

Within-person pain variability alone exceeds standard responder thresholds for pain.

3-point change

Pain intensity (1-10)

Pain Group — Healthy — Acute — Chronic

n = 219

Pain Intensity (0-10 NRS)

*Gunsilius, Heffner, Petzschner, **in prep***

What we need: measures of brain function.

Example Computational Psychiatry
Computational measures predict better than behavior and brain imaging alone.

*Huys et al., **Nature Neuroscience**, 2016; Stephan et al., **Neuron**, 2015; Brodersen et al., **PLoS CB**, 2011; Wiecki et al., **PLoS ONE**, 2016; Wiecki et al., **Clinical Psychological Science**, 2015*