

# ANTICIPATING MANIC AND DEPRESSIVE SHIFTS

in patients with bipolar disorder using early warning signals

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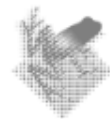
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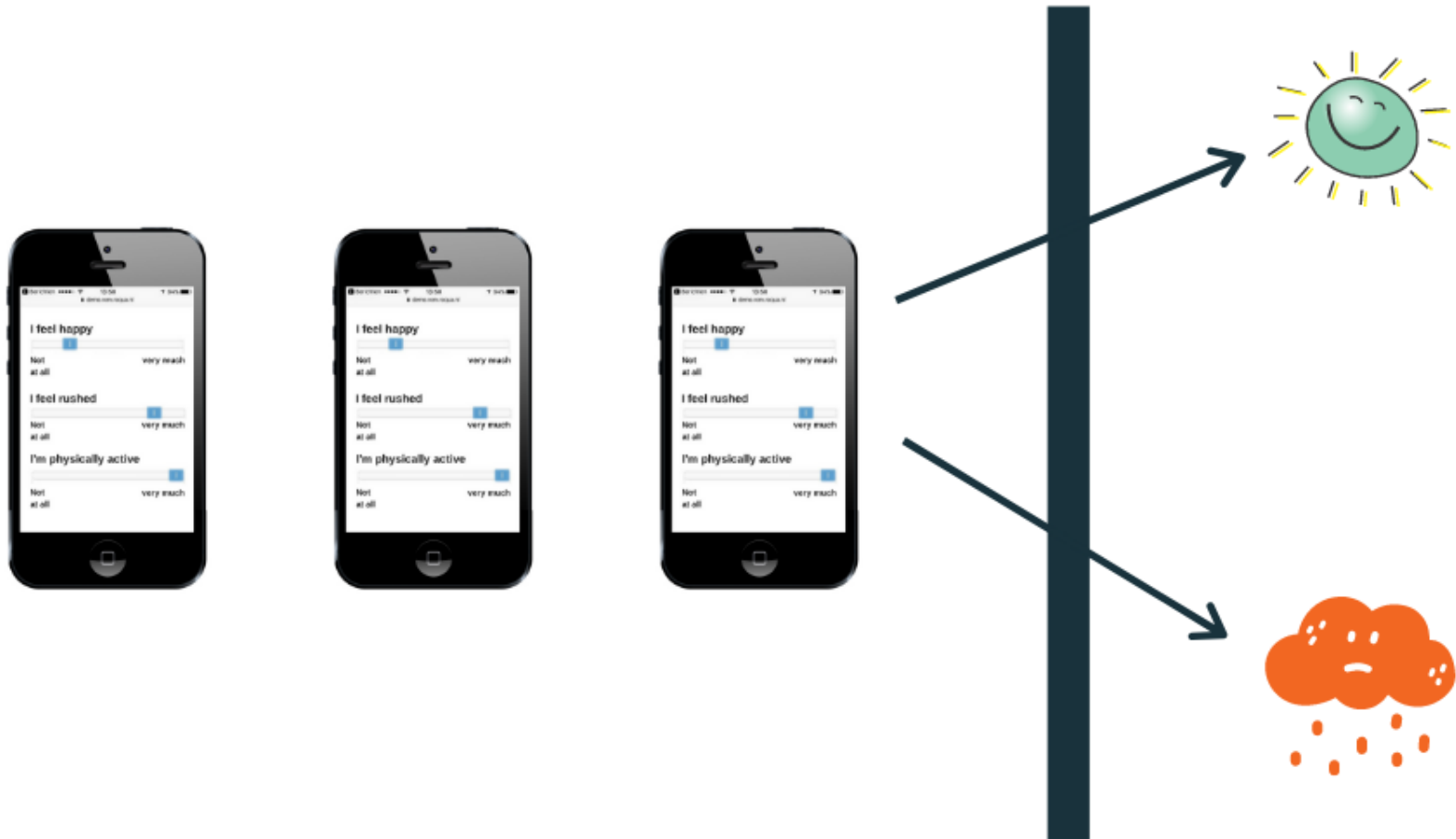
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# Can we anticipate transitions in bipolar disorder?

And does this have clinical utility?



# Sample and ESM/EMA monitoring

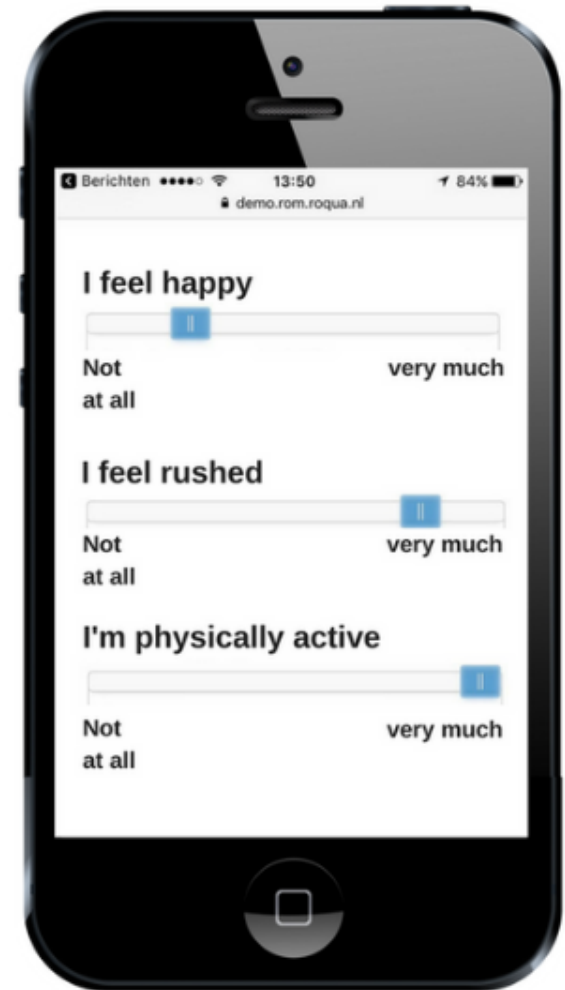
**20 patients with bipolar disorder** type I/II  
(rapid cycling)

**5X DAILY**

ESM/EMA questions on mood  
and symptoms

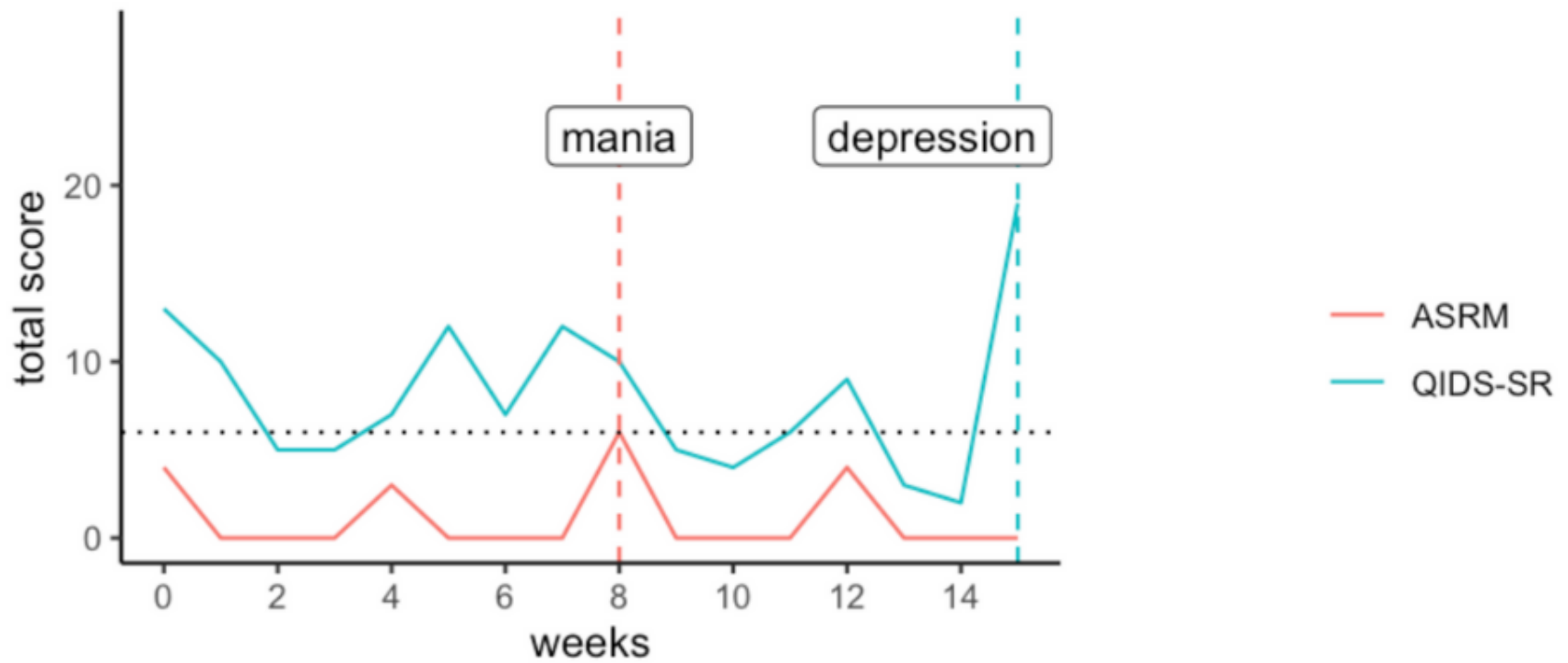
**WEEKLY**

Depressive and manic  
symptom questionnaires



# Definition of transitions

- Abrupt transitions to mania or depression: 6-point increase in 1 week



# Approach

- Focused on **17** EMA/ESM affective states and symptoms
- Early warning signals estimated in moving windows
  - Rises in the autocorrelation at lag-1
  - Rises in the variance

## Preprocessing steps

- Outliers winsorized
- Detrending with Gaussian kernel smoothing function over the whole pre-transition period
- Missing data not imputed



# EWS calculation

- Window size: 2 weeks (70 observations)
  - Sensitivity analyses at 1, 2, and 3 weeks: robust results
- EWS indicators calculated over residuals
- Kendall's tau to test for significant rise in last 2 weeks prior to transition
- Hamed-Rao correction to correct for dependency between nearby windows (Hamed & Rao, 1998)
- Correction for multiple testing with false discovery rate (Benjamini & Hochberg, 1995)

# Clinical utility of EWS

- Positive and negative predictive values
  - PPV: probability of a transition given EWS
  - NPV: probability of no transition given no EWS
- Compared against the prevalence of transitions in this sample
  - 32% mania (no transition 68%)
  - 36% depression (no transition 64%)



**11**

**patients**

with transitions



**8**

**transitions**

Depression



**7**

**transitions**

Mania



**9**

**patients**

No transition



**7**

**patients**

Stable



**2**

**patients**

Unstable



11

patients

with transitions



8

**transitions**

Depression



7

**transitions**

Mania



9

patients

No transition



7

**patients**

Stable

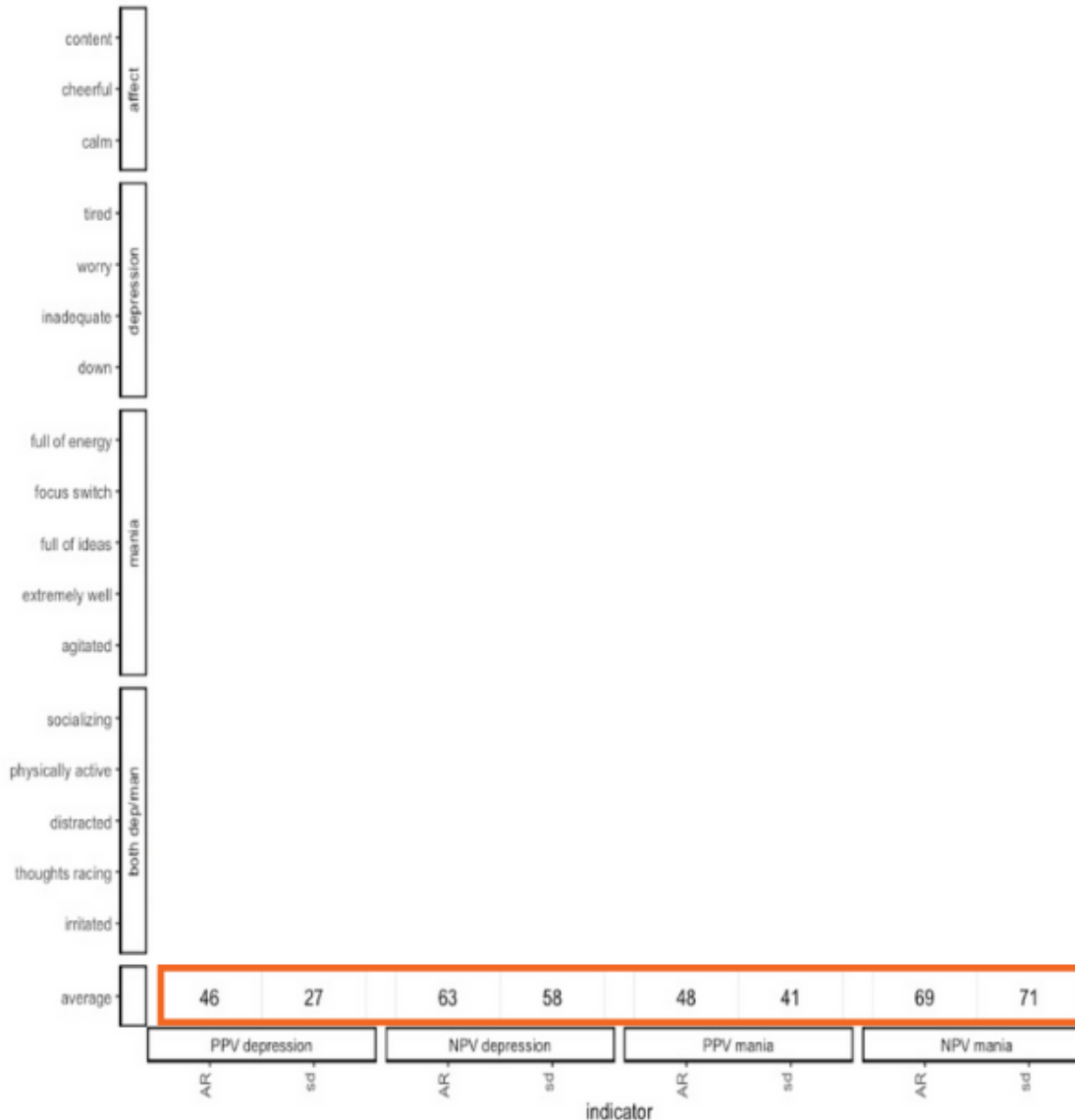


2

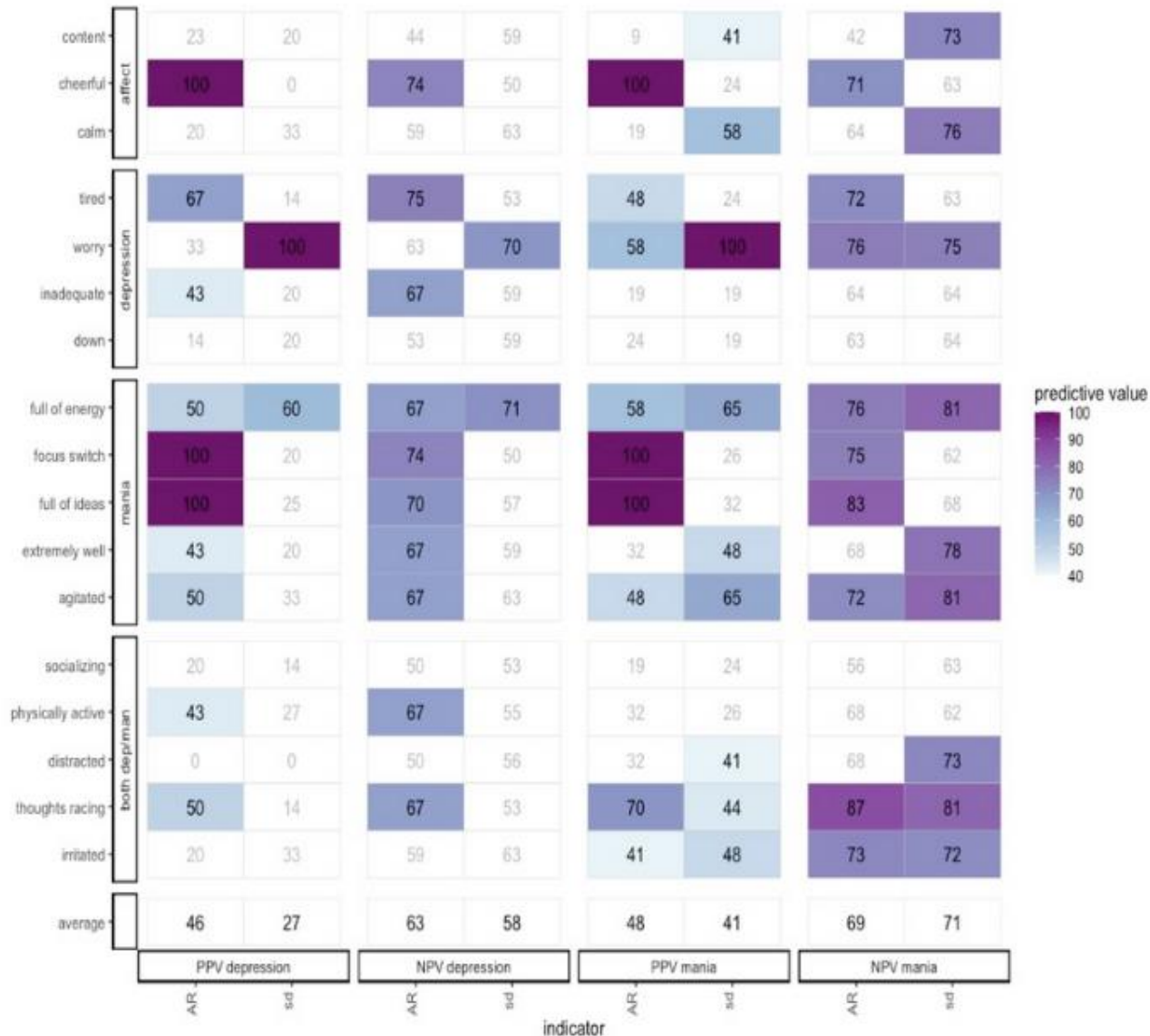
**patients**

Unstable

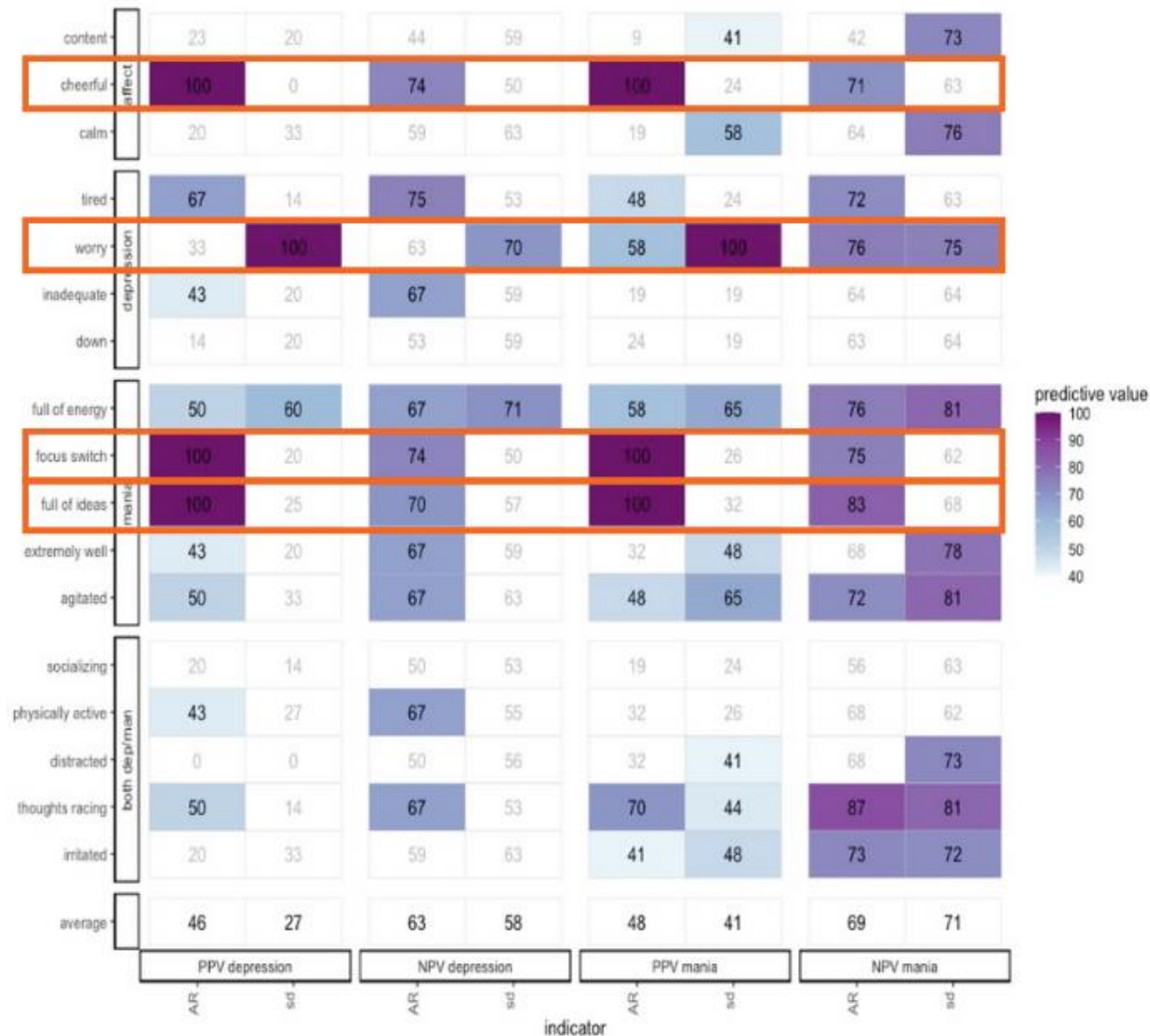
# Can EWS anticipate a manic or depressive transition?



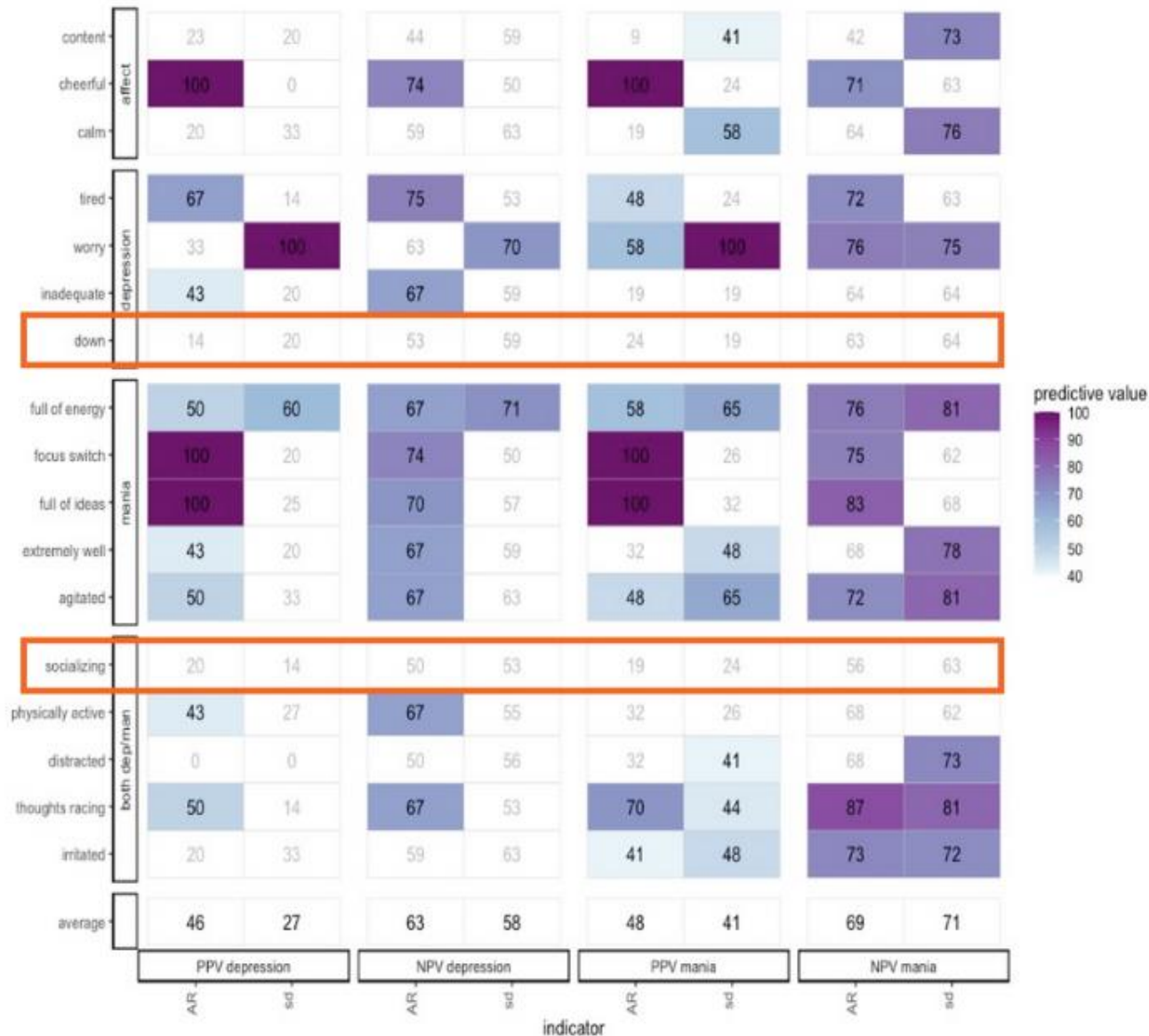
# Can EWS signal a manic or depressive transition?



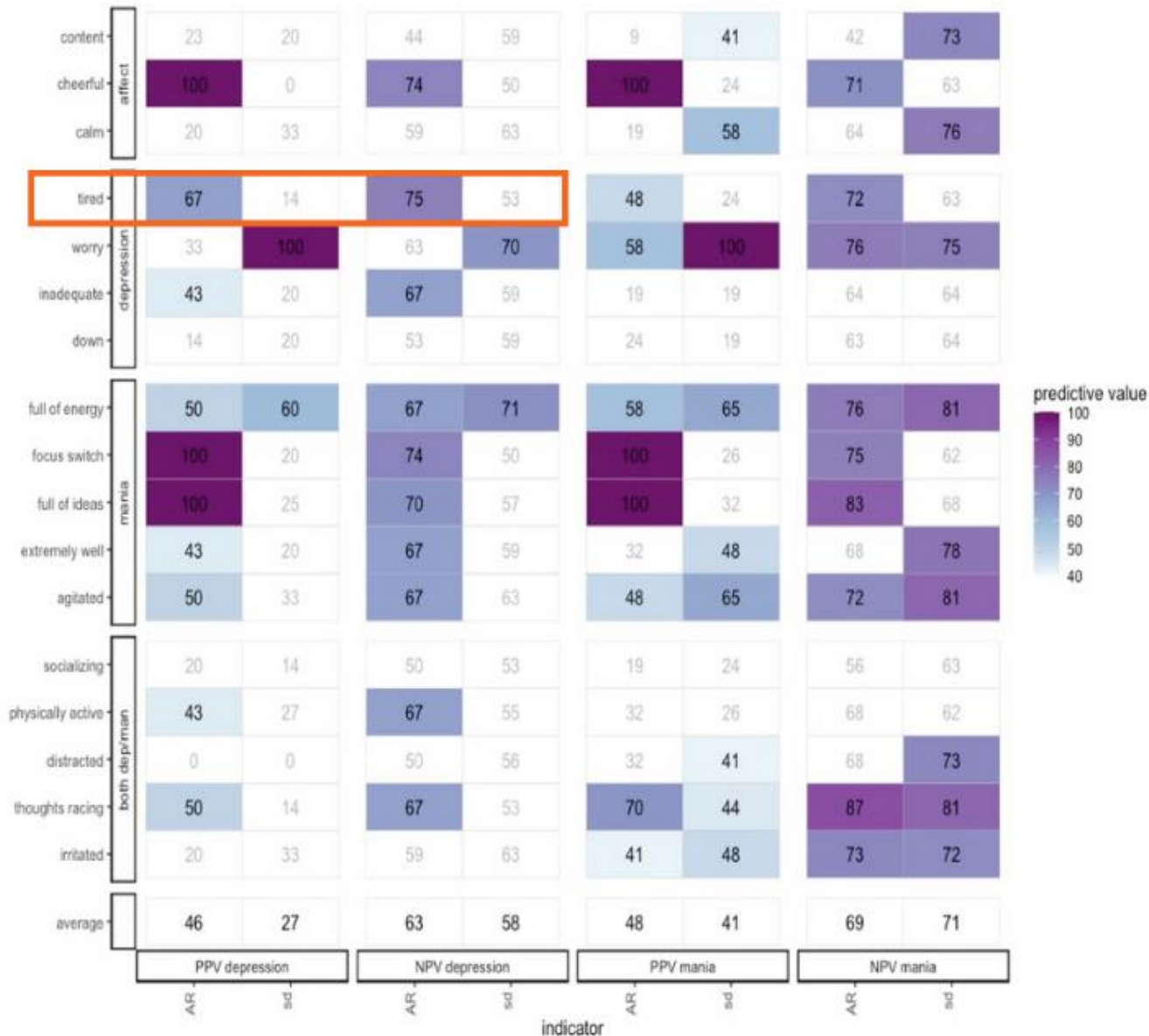
# Momentary states with high predictive value



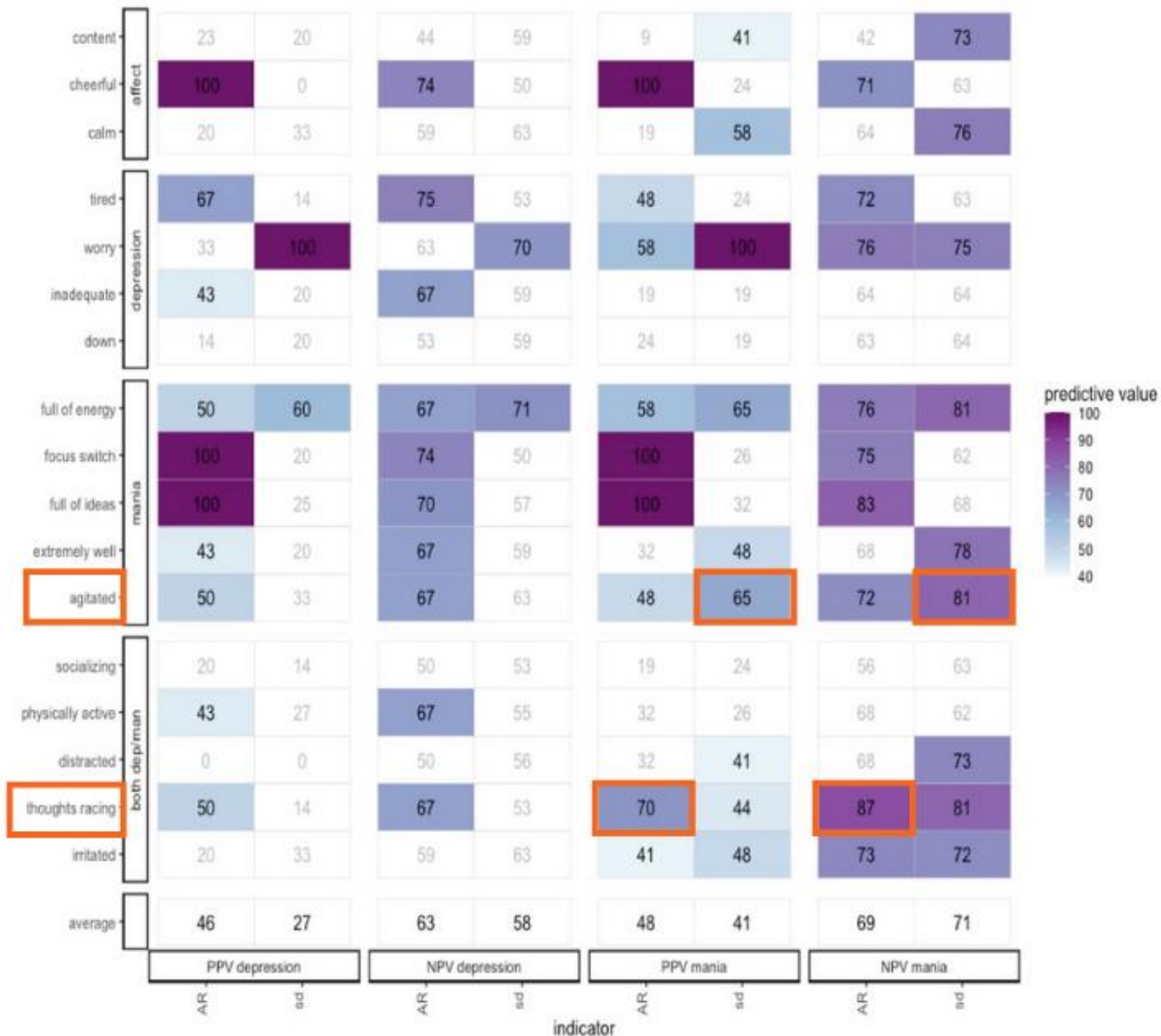
# Momentary states with high predictive value



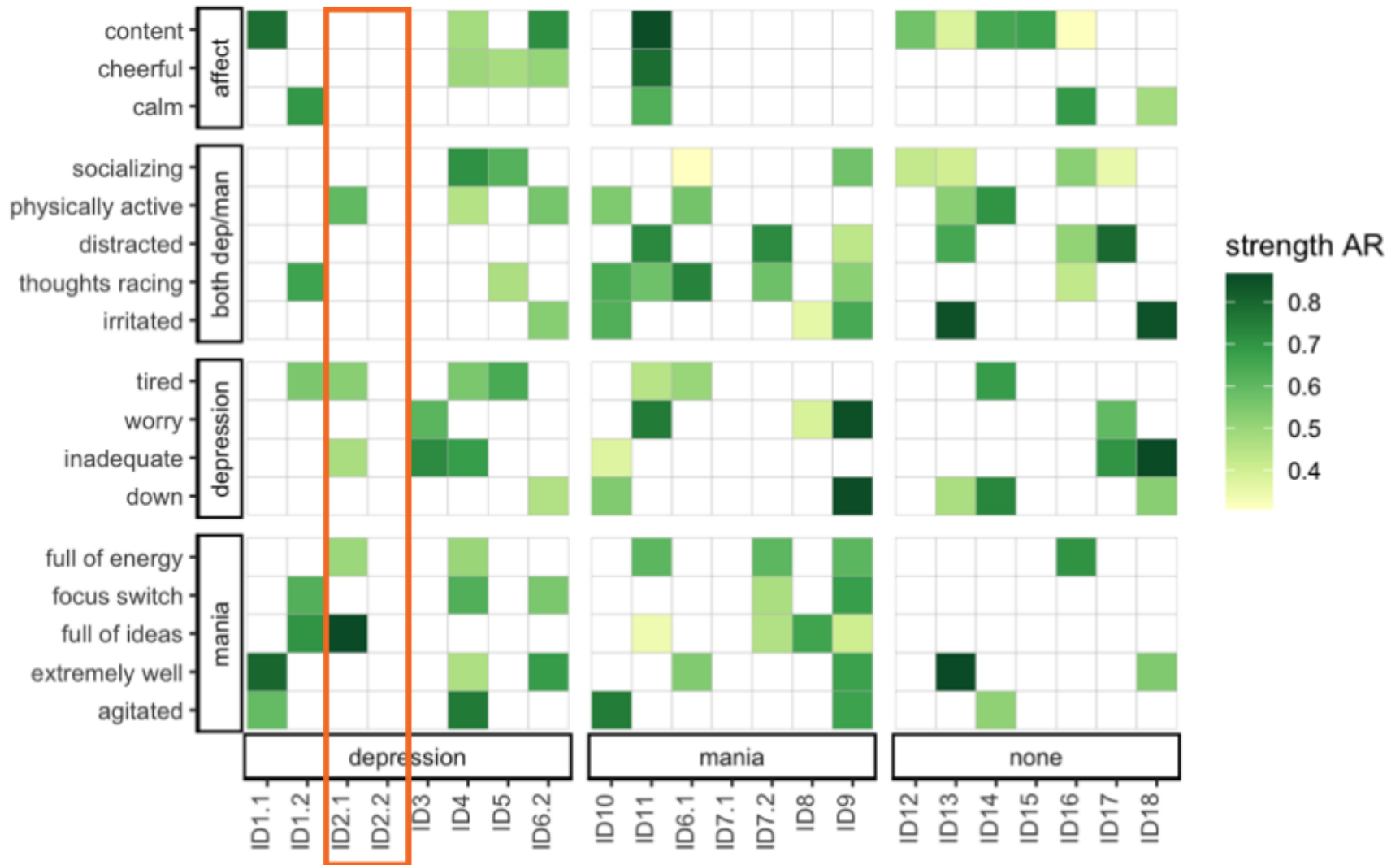
# High predictive value for depression



# High predictive value for mania



# Individual differences in EWS



# **DISCUSSION & CONCLUSION**


- Early warning signals might have clinical utility
- Symptoms/mood states differ in their predictive value
- Large (inter- and intra-)individual differences
- Are EWS detectable in rapid cycling?
- Generalizability to more stable bipolar patients?



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# Individual differences in EWS

