Development of a novel transdiagnostic predictor of psychiatric hospitalization using early trajectories of the Clinical Global Impression Scale

Maxime Taquet[1,2], Kira Griffiths[3], Emily OC Palmer[3], Sheryl Ker[3], Christian Liman[3], Soon Nan Wee[3], Mayowa Oyesanya[3], Scott H Kollins[3,4], Rashmi Patel[5*]

1. Department of Psychiatry, University of Oxford, Oxford, UK., 2. Oxford Health NHS Foundation Trust, Oxford, UK., 3. Holmusk Europe Ltd., London, UK., 4. Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine, Durham, North Carolina, USA., 5. Department of Psychological Medicine, King's College London, Institute of Psychiatry Psychology and Neuroscience, London, UK.

BACKGROUND

- Existing predictors of psychiatric hospitalization are often limited to specific diagnoses or clinical scenarios.
- The Clinical Global Impression – Severity (CGI-S) is a 7-point measurements of illness severity[1] that can be used across psychiatric diagnoses and is frequently recorded in routine clinical practice.
- This study proposed an operationalization of clinical instability based on individual-level fluctuation in Clinical Global Impression – Severity (CGI-S) scores.
- We then investigated whether early instability of CGI-S scores predict risk of psychiatric hospitalization over a 6 month-follow-up period.

METHOD

- This retrospective cohort study using NeuroBlu[2] version 21R1 (Figure 1) a real-world data repository containing de-identified electronic health record (EHR) data from US mental healthcare providers.

Inclusion criteria
- An ICD-9 or ICD-10 code of major depressive disorder (MDD), bipolar disorder, generalized anxiety disorder (GAD), post-traumatic stress disorder (PTSD), schizophrenia or schizoaffective disorder (SCZ), attention deficit hyperactivity disorder (ADHD), or personality disorder (PD).
- At least 5 recorded CGI-S scores within a 2-month period, termed the index period.

Exclusion criteria
- Record to hospitalization before or within the index period.

Statistical analysis
- The relationship between clinical instability and risk of psychiatric hospitalization was investigated using Cox regression.
- The primary outcome was any inpatient visit within 6-months following the index period (Figure 2).
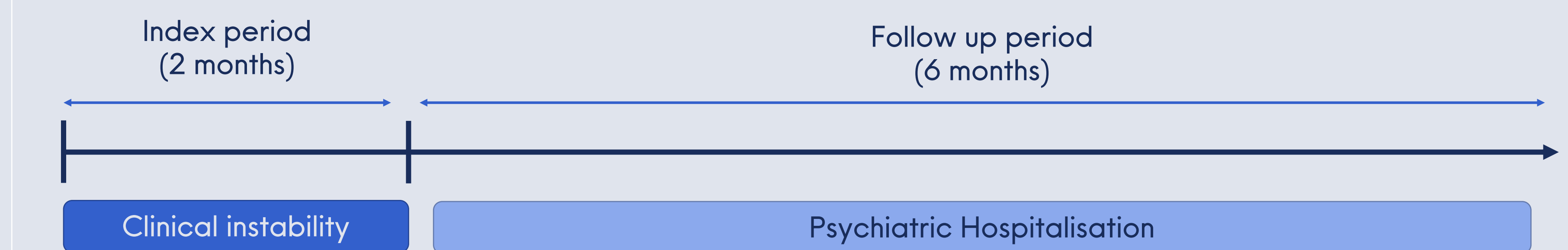

Figure 2. Schematic of study timeline. Clinical severity (mean CGI-S) and clinical instability were measured in a 2-month index period. The outcome of psychiatric hospitalization was evaluated in the subsequent 6-month follow up period.

OPERATIONALIZING CLINICAL INSTABILITY

- Clinical instability was the exposure of interest and this was defined as the generalized root mean squared subsequent differences (RMSSD).
- The root mean squared subsequent differences (RMSSD) is a measure of time-series instability and has been previously used in psychiatry research.[3,4]
- The conventional RMSSD assumes that all recorded values are equally separated in time. This is often not the case in EHR data, where the time between subsequent clinical encounters may vary.
- To account for differences in intervals between subsequent CGI-S measurements, the RMSSD was generalized.

The RMSSD was generalized as follows:

$$tRMSSD = \sqrt{\frac{1}{N} \sum_{i=1}^{N-1} \left(\frac{C_{i+1} - C_i}{t_{i+1} - t_i} \right)^2}$$

where C_i ($i=1,..., N$) are the N measurements of CGI-S and t_i ($i=1,...,N$) are the timestamps at which measurements were recorded, so that $t_{i+1}-t_i$ is the difference in time between two subsequent measurements. This generalization boils down to the original RMSSD if all $t_{i+1}-t_i$ are equal.
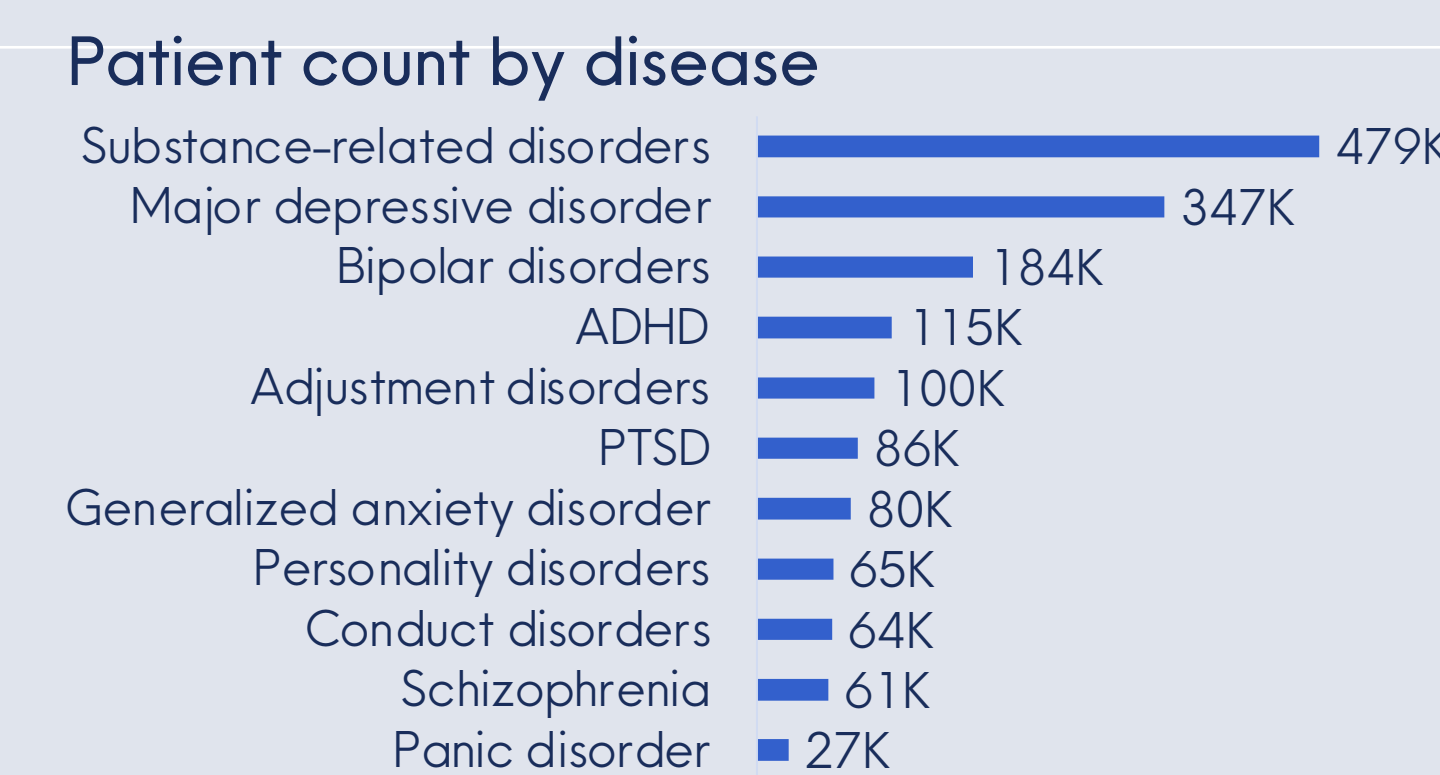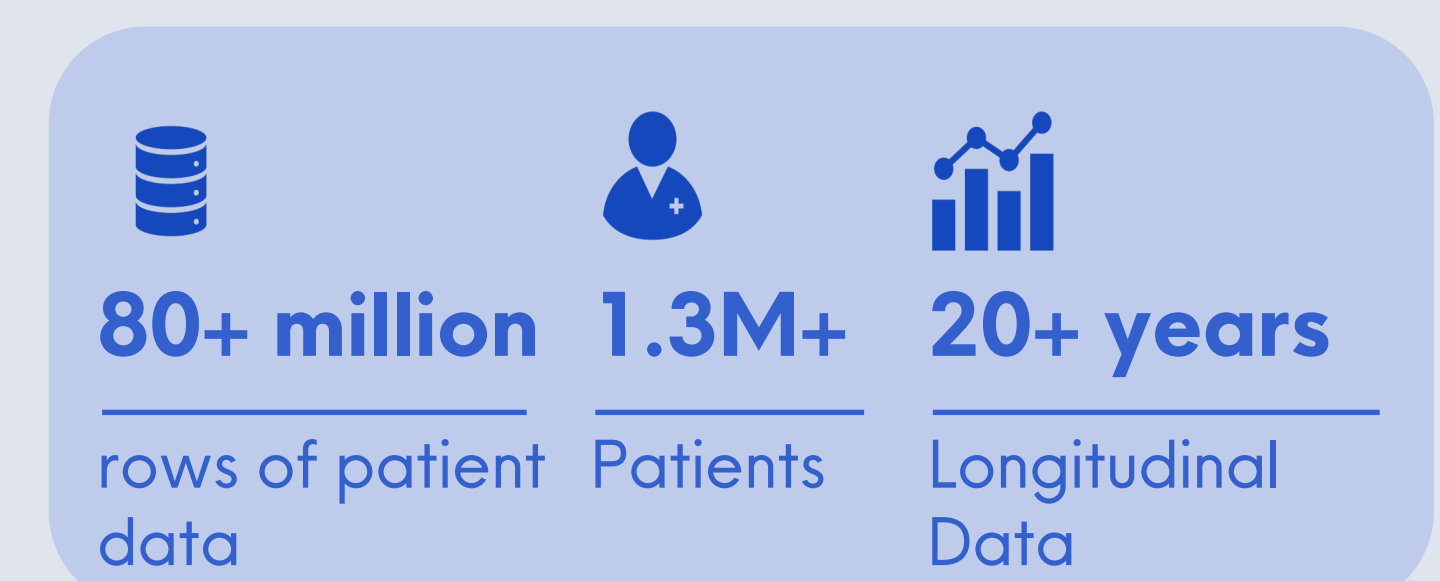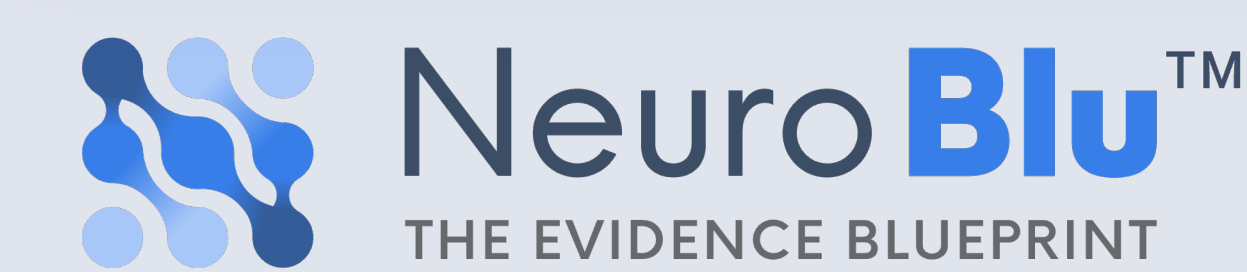

Figure 1. NeuroBlu Database

RESULTS

- A total of 36,914 patients were included (mean [SD] age: 29.7 [17.5] years; 57.3% female).
- The median follow-up time was 180 days; interquartile range = 101-180 days.
- Clinical instability was associated with increased risk of psychiatric hospitalization (hazard ratio: 1.09, 95% CI 1.07-1.10, p<0.001). There was no violation of the proportionality assumption (Chi²=0.62, P=0.43).
- These associations were consistent across all psychiatric diagnoses. The association was more marked among patients with ADHD and GAD, for whom an increase in clinical instability by 1 SD was associated with an 11% increased risk of hospitalization within the next 6 months (P<0.0001). The association was weaker (although still statistically significant) for BD (HR 1.05, 95% CI 1.006-1.09, P=0.025) and SCZ (HR 1.07, 95% CI 1.004-1.14, P=0.038). Associations were also consistent across gender and age groups.

CONCLUSION

- We develop a novel measure of clinical instability using fluctuation of consecutive CGI-S measurements.
- Clinical instability may serve as a transdiagnostic clinical phenotype that provides information complementary to clinical severity and could improve outcome prediction in real-world clinical practice.

Limitations
- Limited definition of hospital admission: we could not distinguish between voluntary and involuntary. Further, only first admissions were captured and therefore we do not know the impact of clinical instability on recurrent hospital admission.

References:
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