Predictors of Functional Impairment in Bipolar Disorder: Results from 13 Cohorts from Seven Countries by The Global Bipolar Cohort Collaborative

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'Everyday' function in Bipolar Disorder

- Bipolar disorder (BD) is a highly impairing mental health condition globally[1].
- The BD-related factors that contribute to functional impairment are not fully understood but include (are not limited to):
  - *Affective (depression, mania) symptoms[2],*
  - *High rates of comorbid psychiatric[3] and medical disorders[4–6],*
  - *Substance abuse[7],*
  - *Sleep disturbance[8],*
  - *Cognitive impairment[9]*
- In order to promote full recovery for everyone, we need a better understanding of the diverse, key predictors of functional impairment in BD.
- Chart a clearer path to interventions.

Barriers to Improving Functional Capacity

- **BD is heterogeneous:** may drive partial response and treatment resistance.
- **BD is a highly comorbid disease:** mental health, environmental comorbidity adds to complexity of the illness and risk for shortened lifespan.
- **BD is a dynamic illness:** periods of acute mood symptoms vs. stability > illness recurrence may affect the brain (e.g., cognitive & functional impairment).
- **Resources for BD research remain insufficient:** compared to other major psychiatric disorders[10].

The Global Bipolar Cohort Collaborative

Set the stage:

- Establish a world-wide research collaborative and cohort of individuals with BD.

Goal:

- Measure the influence of key factors on community function in multiple cohorts of well-characterized BD patients from around the world and to collate and compare results.

Methods

- Thirteen cohorts were included in this study from 7 different countries, totaling 5882 BD patients across sites.
- Find consistencies across samples and identify where differences exist by individual site.
- Multiple cohort replication and expansion approach.
- Each site performed a logistic regression analysis with empirically derived "good versus poor function" as the dependent variable and selected clinical and demographic variables as predictors.

Results

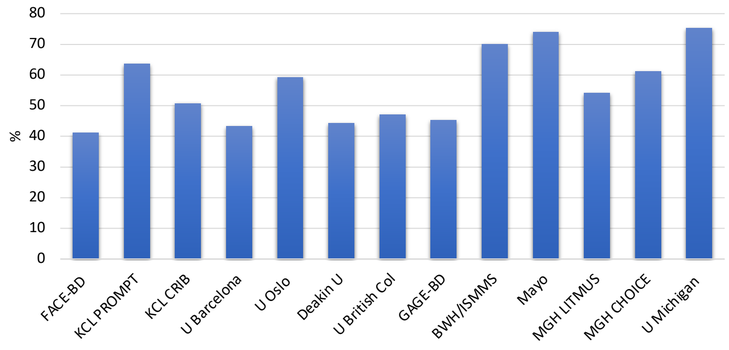
Table 1. Defining functional impairment

Site Name	Country	Poor function defined
FACE-BD (Fondation FondaMental)	France	FAST≥21
University of Michigan	USA	Best Estimate Illness Impact ≥2
King's College London PROMPT	England	WSAS ≥20
King's College London CRIB	England	FAST ≥21
University of British Colombia	Canada	MSIF ≥4
University of Barcelona	Spain	FAST≥21
Deakin University	Australia	GAF≤60
Mass General Hospital LITMUS	USA	LIFTRIFT ≥14
Mass General Hospital CHOICE	USA	LIFTRIFT ≥14
Mayo Clinic	USA	Not working full time
Oslo University Hospital	Norway	GAF <60
GAGE-BD (consortium)	USA	GAF≤60
BWH/ISMMS	USA	WHODAS >5

Table Legend: Functional Assessment Short Test (FAST); Work and Social Adjustment Scale (WSAS); Multidimensional Scale of Independent Functioning (MSIF); Global Assessment of Function (GAF); Longitudinal Interval Follow Up Evaluation-Range of Impaired Functioning Tool (LIFE-RIFT); WHO Disability Adjustment Scale (WHODAS); Best Estimate of Illness Impact from Diagnostic Interview for Genetic Studies (DIGS).

Definitions of functional impairment varied between sites > some used detailed questionnaires and others used work status. Each site defined "good/poor" functioning by using pre-defined cutoffs, medians splits, etc.

Figure 1. Rate of functional impairment by site



The prevalence of "poor" functioning across sites ranged from 41-75%. Although different measures were used at nearly every site, these estimates are consistent with prior literature reporting high rates of disability in BD.

Table 2. Regression results by variable

Variable	Sites reporting significance	Direction of results
Age	1/13 (8%)	Older age→ more impairment
Sex	2/13 (16%)	Female→ more impairment
Race	0/8 (0%)	---
Education level	3/12 (25%)	Lower education→ more impairment
BD subtype	3/12 (25%)	BD I and SZA/BD → more impairment
Psychosis history	3/11 (27%)	Mixed direction: 2 sites Psychosis hx → more impairment; 1 site Psychosis hx → less impairment
Current depressive sx	10/12 (83%)	More severe depression → more impairment
Current manic symptoms	2/11 (18%)	More severe mania → more impairment
Age at onset depression	0/6 (0%)	---
Age at onset mania	0/6 (0%)	---
# Prior manias	2/7 (29%)	More prior episodes → more impairment
#Prior depressions	2/8 (25%)	More prior episodes → more impairment
# Total episodes	0/2 (0%)	---
Comorbid substance dx	2/8 (25%)	Comorbid substance use d/o → more impairment
Comorbid anxiety diagnosis	3/6 (50%)	Comorbid anxiety d/o → more impairment
Global cognition (g)	1/6 (17%)	Lower g → more impairment
Premorbid IQ	0/5 (0%)	---
Lithium	1/6 (17%)	Lithium use→ less impairment
Anticonvulsants	2/6 (33%)	Anticonvulsant use → more impairment
Antipsychotics	3/7 (43%)	Antipsychotic use→ more impairment
Antidepressants	0/7 (0%)	---
Benzodiazepines	0/6 (0%)	---
# psychotropic meds	2/7 (29%)	More psychotropic meds→ more impairment

- A survey of existing data, **compared diverse cultural cohorts**, identified the challenges inherent to conducting research in this area, and **emphasized the need for future collaborative work**.
- **Several key factors** were confirmed to associate with poor outcome across multiple cohorts: education, subthreshold depressive symptoms, comorbid substance and anxiety d/o, medication load.

Summary

Results:

- Results are **largely confirmatory**.
- Highlights the **complex nature of this illness.**

Next steps:

- Needed: a **large-scale, worldwide, prospective longitudinal study** focused squarely on BD and its heterogeneous presentations.

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