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## Improving Diagnostic Delays in Bipolar Disorders in Clinical Practice

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**Running Head:** Diagnosis Delay in Bipolar Disorder

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## INTRODUCTION

A series of worldwide reports have informed that around 70% of the people affected by Bipolar Disorders (BD) need to wait approximately eight years between their first consultation (FC) and the moment that they receive the appropriate diagnosis<sup>1</sup>. In the last years, several clinical markers were identified<sup>2</sup> and educational initiatives among mental health professionals<sup>3</sup> were conducted in order to reduce diagnosis delay (DD).

To the best of our knowledge, the impact of these actions on the ability of physicians to make a timely BD diagnosis at a clinical level has not been investigated.

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## RESULTS AND DISCUSSION

### Diagnostic Timelines

We included 188 patients. Mean age was 38.8 years (SD:12.2, IQR: 17) and mean educational level was 15 years (SD:3.6). 117 were diagnosed as BD I (62.2%) and 70 as BD type II (37.8%). Additionally, 52.4% of the patients experienced psychotic symptoms and experienced a mean number of 5.8 depressive episodes (SD:3.5) and 5.2 manic episodes (SD:3.2).

The mean DD - as defined by the time since the FC until a diagnosis of BD was reached - was 7.6 years (SD: 8.9, IQR: 10.5 years). Overall, DD was longer in BD type II by approximately 6 years ( $t=9.58$ ,  $p<0.001$ ).

A prior erroneous diagnosis was given to 137 patients (72.8%). In almost all cases, the BD diagnosis was made by a psychiatrist ( $n=177$ , 94.1%). Finally, patients with BD type II consulted with an average of 4.1 professionals until receiving a BD diagnosis while BD type I patients 3.4 ( $t=11.5$ ,  $p<0.001$ ). The most common prior diagnoses were major depression (68.4%), followed by personality disorder (16.9%) and schizophrenia (12.5%).

### Time trends in BD diagnosis delay

By including current age at the moment of diagnosis in the model, we found that per year increase, the HR for a timely diagnosis decreased (HR: 0.92, 95% CI = 0.91 to 0.94, HR for a decade increment = 0.43) suggesting that the hazard for a timely diagnosis among patients 10-years older was 57% lower. Table 1 shows clinical and demographical differences among birth cohorts. Adjusting for all variables in Table 1 did not alter our results (HR: 0.87, 95% CI = 0.85 to 0.90). We found consistent results by using negative binomial models.

Figure 1. shows the DD experiences for each birth cohort for time from FE and FC to BD diagnosis, PSO to FC and FC to TMS. The birth cohort effect was statistically significant for all comparisons, but the effect is less pronounced for PSO to FC (Table 2).

## Discussion

The present report shows that there is evidence to suggest that physicians are improving their clinical capacities to diagnose BD timely. We have shown that there is a significant birth cohort effect in the time since FE to correct diagnosis, time since FC and correct diagnosis and time since FC to TMS, even after correcting by potential differences in clinical presentation of these patients over the years. A smaller effect is seen in PSO to FC which is a delay strictly dependent on the patient and its environment. Consequently, efforts should still be directed to shorten this latency that did not experience the same improvement. Finally, evidence consistent with an acceleration in the age at first episode was observed<sup>4</sup>.

However, it must be considered for the interpretation of these results that two of the included centers are specialized in mood disorders and that older patients might recall exact dates with greater uncertainty. Furthermore, this data is insufficient to clearly separate between “diagnostic (detection) delay” or a “taxonomic delay” (i.e., patients with a depressive index episode take around a decade to experience their first manic episode)<sup>5</sup>.

In conclusion, DD could be improving over the last decade.

### KEY MESSAGE

In the last twenty years, worldwide reports have signaled that two out of three people suffering from Bipolar Disorders need to wait for an average of 8 years to receive an appropriate diagnosis and treatment. This study suggests that, for the first time, these delays might be improving.

### LEARNING POINTS

- We show that the time from first episode to correct diagnosis, time from first consultation to correct diagnosis and mood stabilizer initialization have shortened in the last years.
- This effect was evident even after accounting for differences in clinical presentation over the years.
- These results come from mood disorders specialized centers, which suggests that training and educational interventions could improve diagnostic performance.

## **METHODS**

Patients diagnosed with BD from four psychiatric centers in Buenos Aires, Argentina; Jujuy, Argentina; Santiago, Chile; and Asunción, Paraguay were recruited to participate in the present study from January 2015 to 2017. Patients presented BD type I, or II based on the Diagnostic and Statistical Manual of Mental Disorder (DSM-IV) and a follow-up of more than 36 months. Exclusion criteria were: current substance abuse, mental retardation, neurological disease, or any unstable clinical condition. Late-onset BD were also excluded.

### **Instrument**

DD was assessed through a semi-structured interview that assessed: age of perceived symptom onset (PSO), age at first full-blown mood episode (FE), date of FC, type of first professional visited (i.e., general practitioner, psychiatrist, psychologist), date of confirmed diagnosis, alternative diagnoses considered, and medical specialty of the physician diagnosing BD. Data on the total number of professionals seen until diagnosis of BD was reached, type of professional that made the correct diagnosis, type of medications received and the delay until the first mood stabilizer were also recorded (TMS). Additional data were collected, when necessary, from clinical records.

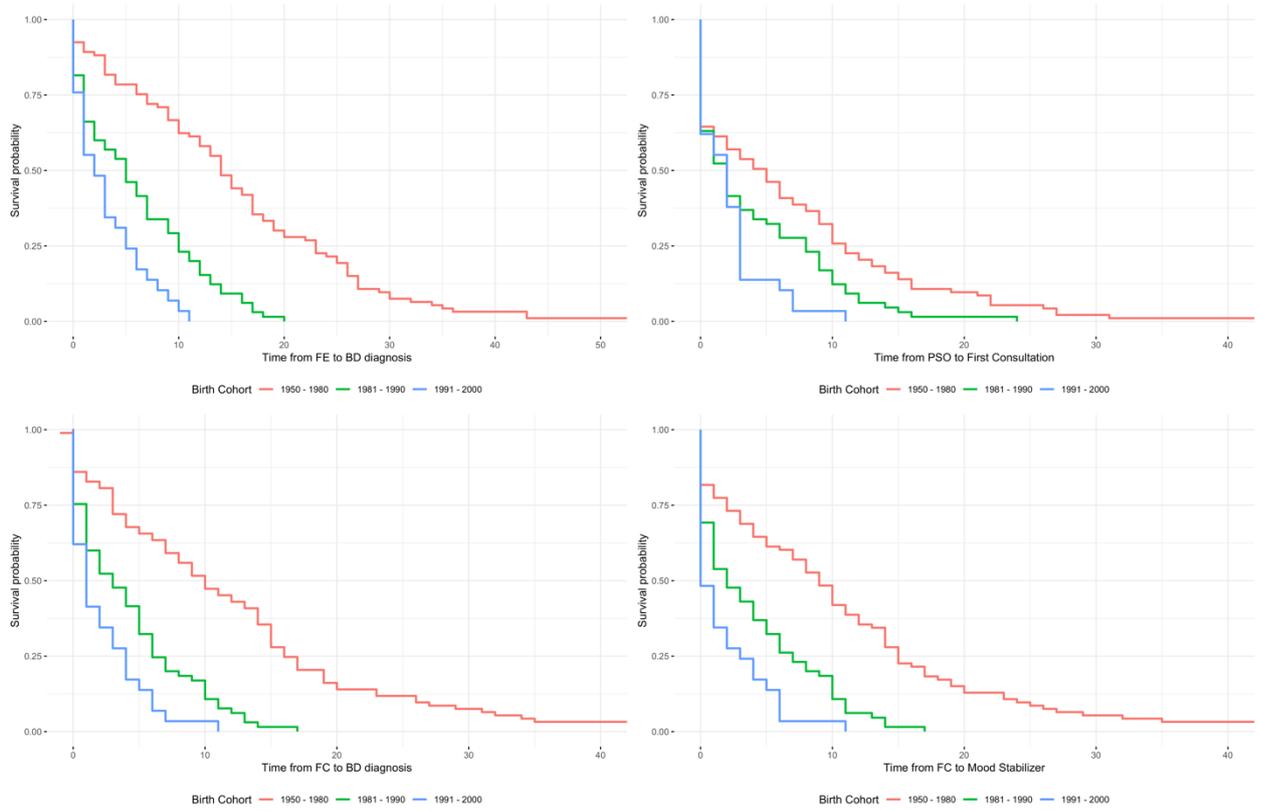
### **Statistical analysis**

Frequencies, averages, medians, interquartile ranges (IQR), and standard deviations (SD) were used to describe demographic or clinical data and diagnostic timelines.

A Cox proportional hazard regression model was used to observe whether a time-trend in DD was observed by including age at the time of the interview in the model. Hazard ratios (HR) greater than 1 are interpreted as indicating that the presence of that covariate is associated with a shorter period of time until the event of an appropriate diagnosis of BD. We tested the proportional hazards assumption using log-log plots and Schoenfeld residuals. To assess the robustness of our findings, we replicated the analyses using a generalized linear model assuming negative binomially distributed counts for the number of specialists seen before a correct diagnosis was made for the same models.

All analyses were performed using R statistical software (version 3.4.1).

**Figure 1.** Birth Cohort Effect showing the survival experiences for each cohort



FE = first full-blown mood episode; PSO = Perceived Symptom Onset; FC = First Consultation; BD = Bipolar Disorders.

**Table 1.** Clinical, demographic and diagnostic delay characteristics of included patients according to their Birth Cohort.

Baseline covariate	1950-1980 (N=93)	1981 - 1990 (N=65)	1991 - 2000 (n=29)	p value <sup>a</sup>
Age - years, mean (SD)	48.7 (8.9)	31.6 (2.8)	23.0 (2.7)	< 0.001 <sup>#</sup>
Female sex - %	38.7	29.2	27.6	0.348
Education – years, mean (SD)	15.4 (3.4)	15.4 (3.9)	14.0 (3.2)	0.167
<i>Clinical Features</i>				
First episode Depression - %	72.0	44.6	69.0	0.002 <sup>&amp;</sup>
Age at First Episode - mean (SD)	23.1 (7.3)	19.6 (4.6)	16.8 (3.4)	< 0.001 <sup>#</sup>
Type BD (Type I - %)	54.8	69.2	72.4	0.091
Psychotic Features - %	41.9	63.1	62.1	0.017 <sup>&amp;#</sup>
Substance Abuse - %	16.1	38.5	17.2	0.004 <sup>&amp;</sup>
Rapid Cycling - %	22.6	20.0	24.1	0.884
<i>Median Survival Times (specific diagnostic delays)</i>				
Time from FE to BD (median survival, IQR)	14 (12-17)	5 (2-7)	2 (1-4)	
Time from FC to TMS (median survival, IQR)	9 (7-11)	2 (1-4)	0 (0-2)	
Time from FC to BD (median survival, IQR)	10 (7-14)	3 (1-5)	1 (0-3)	
Time from PSO to FC (median survival, IQR)	5 (2-7)	2 (1-3)	2 (0-3)	

a. Proportions are compared with the Fisher's exact test, means with the ANOVA test.

Abbreviations: SD: standard deviation, BD: Bipolar Disorder

# Significant differences at the 0.05 level between 1950-1980 and 1991-2000 after multiple comparison's correction

& Significant differences at the 0.05 level between 1950-1980 and 1981-1990 after multiple comparison's correction

^ Significant differences at the 0.05 level between 1981-1990 and 1991-2000 after multiple comparison's correction

FE = First Episode, BD = Bipolar Disorder, IQR = interquartile range, FC = First Consultation, TMS = Time to Mood Stabilizer, PSO = Perceived Symptom Onset.

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