An increased risk of developing TD has been associated with factors such as older age, female sex, underlying mental illness, and long-term use and higher doses of antipsychotics. The association of TD with the use of typical versus atypical antipsychotics has also been evaluated, with mixed results. To date, predictive models assessing the joint effect of clinical characteristics on TD risk have not been developed and validated in the US population.

STUDY OBJECTIVE: To develop a prediction model to identify patient and treatment characteristics associated with the occurrence of TD among patients with psychiatric disorders taking antipsychotic medications, using a retrospective database analysis.

METHODS: Adult patients with schizophrenia, major depressive disorder, or bipolar disorder who were taking oral antipsychotics, and who had 6 months of data prior to the index date were identified from Medicaid claims from six US states. The index date was defined as the date of the first claim for an antipsychotic drug after a claim for the underlying disorder but before TD diagnosis. A multivariate Cox prediction model was developed using a cross-validated version of the least absolute shrinkage and selection operator (LASSO) regression method to improve prediction accuracy and interpretability of the model. The predictive performance was assessed in a separate validation set via model discrimination (concordance) and calibration.

RESULTS: A total of 189,415 patients were identified: 66,723 with bipolar disorder, 68,573 with depressive disorder, and 54,119 with schizophrenia. The selected prediction model had a clinically meaningful concordance of 70% and was well calibrated (P = 0.46 for Hosmer–Leme show goodness-of-fit test). Patient's age at index date (hazard ratio [HR]: 1.03), diagnosis of schizophrenia (HR: 1.73), dosage of antipsychotic at index date (up to 100 mg/day chlorpromazine equivalent; HR: 1.40), and presence of bipolar and related disorders (HR: 1.16) were significantly associated with an increased risk of TD diagnosis. Use of atypical antipsychotics at index date was associated with a modest reduction in the risk of TD (HR = 0.94).

CONCLUSIONS: This study identified a group of factors associated with the development of TD among patients with psychiatric disorders treated with antipsychotics. This may allow physicians to better monitor their patients receiving antipsychotics, allowing for the prompt identification and treatment of TD to help maintain quality of life.

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63
Long-term Outcomes with Aripiprazole Lauroxil for the Treatment of Schizophrenia: A 2-Year, Phase 3, Multicenter Extension Study

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ABSTRACT: Background: One of the challenges in schizophrenia long-term trials is that clinical outcomes are often confounded by covert nonadherence to prescribed oral antipsychotics. This is a post hoc analysis (>2 years) of the symptoms and illness trajectory of patients treated with the long-acting injectable (LAI) antipsychotic aripiprazole lauroxil (AL). As adherence to LAIs can be monitored, these data could assess outcome trajectories unaffected by medication discontinuations that may occur with oral antipsychotics.

METHODS: The efficacy and safety of once-monthly AL (441 or 882 mg) for the treatment of schizophrenia were previously demonstrated in a phase 3 trial, followed by a 52-week, long-term safety study of two AL doses (441 or 882 mg once monthly; patients continuing from the phase 3 study remained on their fixed AL dose [NCT01626456]), after which patients could enroll in a second long-term extension study. Patients entering the second long-term study continued on their fixed AL dose, with a variable follow-up period of up to 128 additional weeks (NCT01895452). In this post hoc analysis, the extension studies were combined to provide continuous outcome data over 2 years' follow-up. The 12-week assessment visit (rather than the first visit) in the first extension study was chosen as the baseline to account for patients entering this study with variable AL exposure histories (with/without prior AL exposure). We report on the trajectory of symptoms and illness severity for >2 years (up to 112 weeks) after the 12-week visit using the Positive and Negative Syndrome Scale (PANSS) total and Clinical Global Impression–Severity (CGI-S) scale scores. Course of illness was measured as the difference in PANSS and CGI-S scale scores within dose

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groups from baseline to end of follow-up, analyzed using MMRM.

RESULTS: Overall, 432/478 patients entering the initial 52-week study were included in the post hoc analysis. For the AL 441 and 882 mg groups, respectively, baseline scores (mean ± SD) were 59.91 ± 16.25 and 56.27 ± 12.89 (PANSS), and 2.99 ± 0.97 and 2.79 ± 0.79 (CGI-S scale). Approximately 49% of patients (211/432) remained for the entire 112-week follow-up. Over this period, the trajectory of PANSS scores improved significantly compared with baseline for both the 441 and 882 mg groups, with changes from baseline (least squares mean ± SE) of −5.46 ± 0.92 (P < .0001) and −4.99 ± 0.53 (P < .0001), respectively. CGI-S scale scores had similar improvement: changes from baseline of −0.32 ± 0.07 (P < .0001) and −0.28 ± 0.04 (P < .0001) for the AL 441 and 882 mg groups, respectively. Overall, AL was well tolerated, with a safety profile over a 2-year follow-up that was consistent with the initial 52-week safety results.

CONCLUSION: This post hoc analysis demonstrates the safety and continued therapeutic efficacy of long-term treatment with AL in patients with schizophrenia. There were no apparent dose differences in the trajectory of symptom changes over the course of a 2-year follow-up.

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64
Aripiprazole Long-acting Injectable in Schizophrenia. An 18-month Follow-up and Mirror-image Study

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ABSTRACT: Study Objectives:
1. To assess the effectiveness, functionality and tolerability of Aripiprazole long-acting injectable (ALAI) in patients with stable schizophrenia
2. Compare hospitalizations and emergency assists during 18-month period before (retrospective period) and after (prospective period) switch to ALAI

METHOD: The study sample involved 18 patients with stable schizophrenia (DSM 5 criteria) who started treatment with ALAI between January-December 2016.
Variables: age, gender, psychopharmacological treatment.

TABLE 1. Efficacy, functionality and treatment compliance results

	Baseline	6 Months	12 Months	18 Months
BPRS	20.53 (±3.17)	17.81 (±3.16)	17.46 (±3.11)	17.03 (±3.13)
BPRS-P	6.94 (±1.03)	6.14 (± 1.05)	6.09 (±1.03)	6.16 (±1.07)
BPRS-N	7.96 (±0.73)	6.44 (±0.69)**	6.11 (±0.73)**	6.01 (±0.63)**
I.C.G. S.I	4.24 (±0.83)	3.10 (±0.84)**	3.08 (±0.81)**	3.09 (±0.81)**
PSP	55.95 (±4.05)	63.08 (±5.77)	63.89 (±5.05)	66.33 (±5.37)*
Treatment compliance	100%	66.6%	66.6%	61.1%

*p < 0.05, **p < 0.01

- Follow-up study: Prospective assessments were performed at baseline and at 3, 6, 9, 12, 15 and 18 months:
• Brief Psychiatric rating Scale (BPRS)
• Global Clinical Impression Scale (ICG-SI)
• Personal and social Performance (PSP)
• Side effects reported
- Mirror-image study: 18-month before and after switch
• Number of hospitalizations and emergency assists
The study was performed in accordance with the Declaration of Helsinki and all the participants provided written consent for participation.
Student's t-test and Chi-square test were used to assess differences between baseline evaluation and subsequent visits. For mirror-image analysis test Z and MacNemar was used.

RESULTS:
a) Efficacy and functionality: At the end of the study we observed:
• A statistically significant: reduction in the total score of ICG-SI, and increase in the total score of PSP
• A reduction in the total score of BPRS.
There is an indirect correlation between age and changes in the score on: BPRS and ICG-SI (p < 0.05) and PSP scale (p < 0.05)
b) Tolerability: The most frequent side effect with an incidence of 22% was transient mild insomnia
c) Psychopharmacological treatment: The percentage of patients on monotherapy increased from 39.6% baseline to 66.6%, and treatment with Biperidene decreased from 27.5% to 5.5% at the end of the study
d) Number of hospitalizations and emergency assist:
• 12 hospital admission during 18-month period before switch to ALI, and 3 hospital admission 18-month after switch
• 24 emergency assist during 18-month period before switch to ALI, and 7 emergency assist 18-month after switch
e) Treatment compliance: shown in Table 1.

CONCLUSIONS: ALAI can be effective therapy for the treatment of patients with schizophrenia: improves psychopathological symptoms, functionality and can

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