

**Original Research** 

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#### **CME** Objective

After studying this article, you should be able to:

· Find ways to support medication adherence for patients with schizophrenia

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Antipsychotics for Schizophrenia: Sociodemographic Characteristics and Treatment Adherence

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#### ABSTRACT

Objective: Long-acting injectable (LAI) antipsychotic medications are employed universally for the treatment of schizophrenia. This study retrospectively assessed the variables that factor into an individual's adherence to LAIs.

Methods: The data sample was obtained from the adult ambulatory services of a large general hospital mental health center located in Elizabeth, New Jersey. Reports were run in November 2015 to identify patients who had received at least 1 LAI between January 1, 2014, and October 14, 2015. In September 2016, an additional report was run to collect follow-up data. The sample included 120 women and 178 men, ranging in age from 18-81 years, who received at least 1 LAI during a 23-month period. A hazard analysis for single-decrement, nonrepeatable events was used to assess the risk of discontinuation of LAIs during the study period. Separate  $\chi^2$  analyses were conducted to assess differences in discontinuation rates for sociodemographic variables, program type variables, type of long-acting medication, and time effects.

**Results:** The cumulative continuation rate across the study period was 73%. Main effect differences were found in continuation rates for program type ( $\chi^2_2$ =10.252, P=.006), LAI type ( $\chi^2_5$ =23.365, P<.000), and prescribed frequency of LAI ( $\chi^2_2 = 7.622$ , P = .022). In addition, multiple time-dependent effect differences were found. No significant main effect results were found for LAI continuation rates and patient age ( $\chi^2_3$  = 3.689, P = .297), sex ( $\chi^2_1 = 0.904$ , P = .342), race ( $\chi^2_3 = 5.785$ , P = .123), or enrollment in involuntary outpatient commitment ( $\chi^2_1 = 2.989, P = .084$ ).

**Conclusions:** The findings of the current research suggest that medication type, frequency of medication appointments, and program type may be key in increasing and maintaining LAI adherence.

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ong-acting injectable (LAI) antipsychotic medications for the I treatment of schizophrenia have been described as one of the most potentially useful strategies for enhancing adherence<sup>1</sup> and being "highly efficacious,"<sup>2(p1263)</sup> "an attractive treatment option,"<sup>3(p1249)</sup> and "an important advance in the treatment of schizophrenia."4(p1003) Two of a number of primary advantages reported in the literature for LAIs are verifiable medication delivery and immediate recognition **Clinical Points** 

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- Long-acting injectable (LAI) antipsychotics should not be the last resort for treating schizophrenia.
- Many patients are adherent with LAIs when treated at an outpatient level of care.
- Current research suggests that patients are more adherent with LAIs dosed monthly compared to twice a month.

of medication nonadherence,<sup>5</sup> which are both significant problems in treating schizophrenia.<sup>6</sup> Yet, utilization remains low.<sup>2</sup>

LAIs are said to have an image problem complicated by the tendency to use LAIs as a last resort.<sup>7</sup> While anecdotal explanations point to patient resistance to accepting LAIs, prescriber hesitation<sup>7</sup> and ambivalence<sup>8</sup> are viewed as contributing to the low utilization. The utilization of LAIs needs to be understood in actual practice without the biases inherent in patient clinical trials. For reasons not clearly understood, many patients with schizophrenia are not offered the option of an LAI until after several relapses when a chronic course is unlikely to be reversed.<sup>2</sup>

Limited data are available on the sociodemographic characteristics or service utilization patterns of LAI continuers or discontinuers. A longer duration of previous antipsychotic medication treatment years (10.5) was associated with discontinuation of an LAI for patients with schizophrenia.<sup>9</sup> Age was not associated with continuation in 2 studies<sup>10,11</sup> or being prescribed an LAI,<sup>12</sup> but older patients were associated with continuation in other studies.<sup>13–16</sup> Sex was not associated with being prescribed an LAI<sup>12</sup> or continuing on an LAI,<sup>10</sup> but males were associated with continuation in another study.<sup>16</sup> Racial minorities were found more likely to be prescribed an LAI than nonminority patients.<sup>12</sup> In reference to program status, outpatient status was associated with continuing on an LAI in 2 studies.<sup>11,13</sup> Continuing on an LAI was associated with inpatient status in 1 study<sup>16</sup> and with an outpatient compulsory treatment program in another.<sup>11</sup>

The purpose of the current research is to retrospectively assess the role of several sociodemographic variables, type of long-acting medication, and program type in LAI adherence. The study sought to test variables related to continuation of LAI treatment in an effort to identify LAI consumers who are more likely to continue taking an LAI as well as to identify needed services and supports to enhance adherence rates. Furthermore, salient variables related to continuation may assist providers in making the decision of when and if a patient is a candidate for an LAI.

### METHODS

#### Setting

Trinitas Regional Medical Center (TRMC) operates a large comprehensive community mental health center in Elizabeth, New Jersey. The adult ambulatory services are located across the street from the acute psychiatric emergency and psychiatric inpatient services. Elizabeth is a low-income and ethnically diverse (Hispanic: 59.5%, black: 21.1%, and white: 18.2%) community. Clinic patients are primarily unemployed and on supplemental security income/social security disability (Medicaid, Medicare, or both), with no more than a high school education. Approximately 10% are undocumented aliens. Clinic patients are predominately from Elizabeth and surrounding communities.

#### Data

The current research used data gathered from TRMC's electronic medical record (EMR) system. Reports were run in November 2015 to identify patients who had received at least 1 LAI between January 1, 2014, and October 14, 2015. In September 2016, an additional report was run to collect follow-up data. At the time of the initial EMR report, a sample of 300 patients aged  $\geq$  18 years was identified. For each of the identified patients, demographic data (ie, age, sex, race) and information on clinical services received during the study period (ie, program type, involuntary outpatient commitment [IOC] status, date of first LAI given during the study period, total number of injections received during the study period, and LAIs used) were collected. When the final EMR report was run, additional data were collected on the date each identified patient received their last injection and the date of last mental health clinical contact for services of any kind with TRMC. The resulting data set identified LAI discontinuers and continuers.

#### **Dependent Variables**

*Time.* The 23-month study period was subdivided into six 3-month intervals: 0–3, 4–7, 8–11, 12–15, 16–19, and 20–23 months.

*Adherence.* Adherence was assessed in terms of continuation and discontinuation of LAIs. An LAI discontinuer is defined as any patient who received no additional injections at TRMC after October 14, 2015.

#### Independent Variables

*Sex.* Patients were divided into male and female subgroups. *Age.* Patients were divided into 4 subgroups on the basis of their age at the time of the initial EMR report: 18–30, 31–45, 46–60, and >61 years.

*Race*: Patients were categorized into 4 groups: white, black, Hispanic, and other.

*IOC participation.* Patients were categorized into 2 groups: those who were involved in the IOC services at any point during the 23-month study period and those who were not.

**Program type.** Patients were categorized into 3 mutually exclusive groups: adult outpatient unit, higher level of care, and multiple. Patients in the adult outpatient unit group received only traditional ambulatory outpatient services (ie, medication management, weekly group therapy, occasional individual therapy) during the time they were receiving LAI injections. The adult outpatient unit is a psychiatric unit and does not treat patients with substance use as a primary diagnosis. Patients in the higher level of care group received







only more intensive ambulatory services (ie, acute partial hospital, co-occurring partial hospital, substance abuse partial care, and treatment linkage and coordination partial care) during the time they were receiving LAI injections. Patients in the multiple levels of care group received traditional ambulatory outpatient services and more intensive ambulatory services, often switching back and forth, during the time they were receiving LAI injections.

*LAI type.* All patients were categorized into 6 mutually exclusive groups on the basis of LAI(s) they received during the entire length of the study period: haloperidol, risperidone, fluphenazine, paliperidone palmitate, aripiprazole, and multiple. The last category included all patients who received more than 1 type of LAI during the study period.

**Prescribed frequency of LAI.** Patients were categorized into 3 mutually exclusive groups on the basis of the prescribed

frequency of the LAI: twice a month, monthly, and multiple. Individuals who were prescribed risperidone, fluphenazine, or biweekly haloperidol were in the biweekly group. Patients who received monthly haloperidol, paliperidone palmitate, and aripiprazole were in the monthly group. The multiple category included all patients who received more than 1 type of LAI during the study period.

#### Sample

After a visual review of the data on the initial 300 patients, 2 patients were removed from statistical analysis because they were the only patients who received an olanzapine injection for the full length of the study. The final analyzed sample of 298 included 120 women and 178 men, ranging in age from 18 to 81 years (mean [SD] = 43 [14.917] years). Age distribution was positively skewed (0.26) and negatively kurtotic (-0.88). Breakdown by patient-identified racial group was 43.0% white, 48.3% black, 3.7% Hispanic, and 5.0% other. Of the 298 patients, 115 discontinued receiving LAIs at some point during the 23-month study period. Of the 115 who discontinued, 54 continued receiving services at TRMC after the 23-month study period. The remaining 61 were right censored due to lost contact.

#### Statistics Used

A hazard analysis for single-decrement, nonrepeatable events was used to assess the risk of discontinuation of LAIs over the study period. Graphs of hazard rates by groups were used for exploratory analyses before  $\chi^2$  tests were completed to assess subgroup differences. The assumption of proportionality was met for subgroups of the independent variables sex, race, IOC status, and prescribed frequency of LAI. However, the exploratory analyses did reveal time-dependent effects between the subgroups for the independent variables of age (Figure 1), LAI used (Figure 2), and program type (Figure 3).

#### RESULTS

#### Hazard Analyses

Across all patients, the cumulative LAI continuation rate at the end of the 23-month study period was 0.73 or 73%. The highest proportion of discontinuation occurred within the 16- to 19-month interval (Table 1). A summary of the hazard analysis results for independent variable subgroup continuation rates can be found in Table 2.

#### Subgroup Comparisons

*Sex.* No significant differences were found for LAI continuation rates of males and females overall ( $\chi^2_1 = 0.904$ , *P* = .342, n = 298) or at any specific time intervals.

Age. No significant differences were found for continuation rates of the different age groups overall

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to 19 months ( $\chi^2_1$  = 4.874, *P* = .027, n = 164). *Race.* No significant differences were found for LAI continuation rates between racial subgroups overall ( $\chi^2_3$  = 5.785, *P* = .123, n = 298) or at any specific time intervals.

*IOC participation*. No significant differences were found for continuation rates of IOC and non-IOC patients either overall ( $\chi^2_1$ =2.989, *P*=.084, n=298) or at any specific time intervals.

**Program type.** Significant differences were found for continuation rates of patients in different levels of care

Table 1. Long-Acting Injectable Continuation Rates for Adult Trinitas Regional Medical Center Patients From January 1, 2014, Through October 14, 2015, According to Length of Time

Time	Discontinuers/	Cumulative Proportion of Continuation
Interval, mo	Patients, n <sup>a</sup>	at the End of Each Time Interval
0 to 3	6/298	0.99
4 to 7	8/292	0.97
8 to 11	14/284	0.95
12 to 15	14/270	0.90
16 to 19	19/256	0.81
20 to 23	54/237	0.73
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<sup>a</sup>Discontinuers include both censored and noncensored cases.

**chied PDF on any website**. ( $\chi_2 = 10.252$ , P = .006, n = 298). Specifically, post hoc analyses indicated that continuation rates differed between the outpatient subgroup ( $P_t = 0.801$ ) and both the higher level of care subgroup ( $P_t = 0.653$ ,  $\chi_1^2 = 6.158$ , P = .013, n = 243) and the multiple levels of care subgroup ( $P_t = 0.618$ ,  $\chi_1^2 = 7.431$ , P = .006, n = 221). Also, significant time-dependent effect differences were found between the outpatient subgroup ( $P_t = 0.861$ ) and the multiple levels of care subgroup ( $P_t = 0.732$ ) at the 20- to 23-month time interval ( $\chi_1^2 = 4.025$ , P = .045, n = 188).

*LAI type.* Significant differences were found for continuation rates of patients receiving different LAIs ( $\chi^2_5 = 23.365$ , *P*<.000, n = 298). The multiple significant results of post hoc analyses for different LAIs and time-dependent effect differences are summarized in Table 3.

In addition, exploratory analyses conducted after the hazard analysis indicated a significant difference between the mean (SD) ages for individuals prescribed haloperidol (46.2 [15.04]) and risperidone (41.3 [15.27],  $t_{144}$  = -1.952, P = .05).

**Prescribed frequency of LAI.** Significant differences were found for continuation rates of patients receiving different prescribed frequencies of LAIs ( $\chi^2_2 = 7.622$ , P = .022, n = 298). Specifically, post hoc analyses indicated that continuation rates differed between the monthly subgroup ( $P_t = 0.787$ ) and the biweekly subgroup ( $P_t = 0.633$ ,  $\chi^2_1 = 7.483$ , P = .006, n = 273). There were no significant differences between the monthly and multiple subgroups ( $P_t = 0.725$ ,  $\chi^2_1 = 0.484$ ,

	5.	Cumulative Probability That a Patient Will Continue Taking an LAL at the End of the Time Interval <sup>a</sup>						
Variable	n	0 to 3 Months	A to 7 Months	8 to 11 Months	12 to 15 Months	16 to 10 Months	20 to 23 Months	
			4 to 7 Months			10101910011113	20 10 23 1001111	
Sex		0.00 (1 (0)		0.05 ( ( ( )		0.00 (0.0)		
Male	178	0.99 (1/2)	0.97 (1/4)	0.95 (4/4)	0.90 (3/6)	0.82 (9/3)	0./5 (12/1/)	
Female	120	0.97 (3/0)	0.96 (3/0)	0.94 (2/4)	0.89 (2/3)	0.79 (5/2)	0.7 (11/14)	
Age, y								
18–30	78	0.97 (3/1)	0.93 (2/2)	0.92 (3/3)	0.84 (1/4)	0.76 (5/1)	0.69 (5/7)	
31–45	86	0.99 (0/0)	0.99 (1/1)	0.98 (0/2)	0.95 (1/2)	0.82 (2/3)	0.71 (10/7)	
46–60	94	0.99 (1/1)	0.96 (1/1)	0.92 (3/1)	0.87 (3/2)	0.80 (5/1)	0.73 (6/10)	
>61	40	1.00 (0/0)	1.00 (0/0)	1.00 (0/2)	0.95 (0/1)	0.89 (2/0)	0.84 (2/7)	
Race								
White	128	0.98 (2/1)	0.95 (2/2)	0.94 (4/4)	0.90 (1/6)	0.78 (5/2)	0.68 (13/15)	
Black	144	0.99 (2/2)	0.98 (1/2)	0.96 (2/3)	0.89 (3/3)	0.82 (9/2)	0.75 (9/13)	
Hispanic	11	1 (0/0)	1 (0/0)	1 (0/0)	1 (0/0)	0.91 (0/0)	0.83 (1/1)	
Other	15	1 (0/0)	1 (0/0)	0.93 (0/1)	0.93 (1/0)	0.93 (0/1)	0.93 (0/2)	
Involuntary outpatient								
commitment participation								
Yes	51	1.00 (2/0)	0.96 (0/2)	0.91 (2/2)	0.84 (2/1)	0.73 (3/0)	0.63 (5/4)	
No	247	0.98 (2/2)	0.97 (4/2)	0.95 (4/6)	0.91 (3/8)	0.82 (11/5)	0.75 (18/27)	
Level of care								
Adult outpatient unit	166	0.99 (0/0)	0.98 (1/0)	0.96 (3/4)	0.93 (2/4)	0.86 (6/3)	0.80 (10/20)	
Higher level of care	77	0.97(3/2)	0.93 (2/3)	0.90 (3/4)	0.85 (2/4)	0.74(3/2)	0.65 (6/9)	
Multiple	55	0.98(1/0)	0.98(1/1)	0.96 (0/0)	0.87(1/1)	0.73 (5/0)	0.62(7/2)	
IAI		0120 (170)	0.00 (1, 1)	0120 (0,0)		011 0 (07 07	0.02 (7,2)	
Haloperidol	74	1.00 (0/0)	0.99 (0/0)	0.99 (1/0)	0.97 (0/2)	0.93 (1/3)	0.89 (3/13)	
Risperidone	72	0.99 (3/1)	0.96(1/2)	0.91 (2/3)	0.82(3/2)	0.68 (5/0)	0.55 (9/7)	
Fluphenazine	25	1.00(1/0)	1.00(0/0)	1 00 (0/0)	1 00 (0/0)	0.92 (0/0)	0.84 (2/3)	
Paliperidone palmitate	79	0.99 (0/1)	0.95 (1/2)	0.92 (3/3)	0.86 (2/4)	0.72(0/2)	0.69 (6/4)	
Arininrazole	23	0.95 (0/1)	0.93 (1/2)	0.92 (0/3)	0.00 (2/4)	0.77 (3/0)	0.05 (0/3)	
Multiple	25	1.00 (0/0)	1.00 (0/0)	1.00 (0/1)	0.97 (0/1)	0.83 (1/0)	0.77 (0/3)	
Frequency	20	1.00 (0/0)	1.00 (0/0)	1.00 (0/1)	0.20 (0/0)	0.05 (1/0)	0.72 (3/1)	
Monthly	176	0.98 (0/1)	0.96 (3/2)	0.95(4/4)	0.90(2/7)	0.84 (8/5)	0 70 (0/20)	
Twice a month	170	0.90(0/1)	0.90(3/2) 0.07(1/2)	0.93 (4/4)	0.90 (2/7)	0.04 (0/5)	0.79 (9/20)	
Multiple	97 25	1.00 (0/0)	1.00 (0/0)	1.00 (0/1)	0.07 (3/2)	0.7 + (3/0)	0.03 (11/10)	
multiple	25	1.00 (0/0)	1.00 (0/0)	1.00 (0/1)	0.90 (0/0)	0.05 (1/0)	0.72 (5/1)	

Table 3. Stat	istically Significant χ <sup>2</sup>	Results for Continuation	on Rate Differences by L	ong-Acting Injectable	(LAI) Types Over Time
LAI	Multiple	Aripiprazole	Paliperidone Palmitate	Fluphenazine	Risperidone
Haloperidol					
Cumulative	$\chi^2_1 = 3.769, P = .052 (n = 99)$	NS*	$\chi^2_1 = 8.786, P = .003 (n = 153)$	NS*	$\chi^2_1 = 20.056, P < .0001 (n = 146)$
0 to 3 mo	NS*	NS*	NS*	NS*	NS*
4 to 7 mo	NS*	NS*	NS*	NS*	NS*
8 to 11 mo	NS*	NS*	NS*	NS*	NS*
12 to 15 mo	NS*	NS*	NS*	NS*	NS*
16 to 19 mo	NS*	$\chi^2_1 = 9.397, P = .002 (n = 90)$	$\chi^2_1 = 5.559, P = .018 (n = 134)$	NS*	$\chi^2_1 = 8.047, P = .005 (n = 126)$
20 to 23 mo	NS*	$\chi^2_1 = 6.194, P = .013 (n = 83)$	$\chi^2_1 = 6.194, P = .013 (n = 124)$	NS*	$\chi^2_1 = 12.336, P = .0004 (n = 117)$
Risperidone					
Cumulative	NS*	NS*	NS*	$\chi^2_1 = 6.265, P = .012 (n = 97)$	NS*
0 to 3 mo	NS*	NS*	NS*	NS*	NS*
4 to 7 mo	NS*	NS*	NS*	NS*	NS*
8 to 11 mo	NS*	NS*	NS*	NS*	NS*
12 to 15 mo	NS*	NS*	NS*	NS*	NS*
16 to 19 mo	NS*	NS*	NS*	$\chi^2_1 = 4.728, P = .030 (n = 79)$	NS*
20 to 23 mo	NS*	NS*	NS*	$\chi^2_1 = 4.988, P = .026 (n = 74)$	NS*
Fluphenazine					
Cumulative	NS*	NS*	NS*	NS*	NS*
0 to 3 mo	NS*	NS*	NS*	NS*	NS*
4 to 7 mo	NS*	NS*	NS*	NS*	NS*
8 to 11 mo	NS*	NS*	NS*	NS*	NS*
12 to 15 mo	NS*	NS*	NS*	NS*	NS*
16 to 19 mo	NS*	$\chi^2_1 = 6.034, P = .014 (n = 43)$	NS*	NS*	NS*
20 to 23 mo	NS*	NS*	NS*	NS*	NS*
Paliperidone palmitate	No significant cumulative or time interaction effects	NS*	NS*	NS*	NS*
Aripiprazole	No significant cumulative or time interaction effects	NS*	NS*	NS*	NS*

*P*=.486, n=201) or between the biweekly and multiple subgroups ( $\chi^2_1$ =0.729, *P*=.393, n=122). No significant time-dependent effect differences were found.

#### DISCUSSION

The results indicating higher levels of adherence for the adult outpatient unit subgroup compared to the higher level of care and multiple levels of care subgroups were consistent with previous research.<sup>11,13</sup> This finding may be surprising to those who believe that with increased frequency of contact and more "supportive" services in place, patients will show higher levels of medication adherence. While it is accurate that higher levels of care often do include more patient-prescriber contact, more clinical support and contact with therapists, more face-to-face monitoring, and more psychoeducation, other variables may intervene and lead to lower levels of LAI adherence in higher levels of care. Patients in higher levels of care may have greater symptom severity, which could make LAI adherence less likely. Also, the need to focus on the acuity of the patient's clinical presentation at a higher level of care may limit the time spent by clinicians/prescribers "prepping" patients (eg, introducing LAIs, explaining LAIs, building rapport). This prepping may be crucial in the initial stages of LAI treatment to build commitment while bioavailability is being reached.

Highly significant differences were found in adherence between different LAIs. The highest rate of adherence across

all LAI types was found for haloperidol compared to the second-generation LAIs. Several possible hypotheses for the higher adherence rates for haloperidol can be identified. First, it is possible that patients find the medication to be more effective and therefore continue to take it. Second, the significant difference found between the mean ages for individuals prescribed haloperidol and risperidone suggests a possible age/prescribed medication interaction in the current research. Finally, because the current research looked at only a circumscribed amount of time, it is possible that individuals who were taking haloperidol during the study period had already been stabilized on the LAI by the beginning date of the study, whereas patients who were prescribed risperidone began taking LAIs for the first time during the current study and therefore had not been stabilized. This finding warrants additional research, particularly relative to cost differences.<sup>17</sup>

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There are several explanations for the higher rates of adherence among those receiving monthly injections compared to biweekly injections. One possibility is that the difference may be reflective of the patient's physical or emotional discomfort at receiving more frequent injections. Another possibility could be the increased time commitment of attending biweekly injections. A third possible explanation could be related to prescriber bias. If certain patients are placed on biweekly injections because of the severity of their symptoms, those patients also may not be adherent as previously discussed.

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Regarding time-dependent effect differences, the result suggest that across all variables, continuation rates are similar until patients reach the 12- to 15-month interval. After this time, it is more likely that patients will discontinue on the basis of age, LAI type, and level of care. This finding suggests that once patients have reached at least a year of LAI use, additional steps may need to be taken to ensure continued adherence. The lack of an association between continuation rates overall and the measured sociodemographic variables, age, sex, and race is consistent with other published studies.<sup>10–12</sup>

Finally, high LAI continuation rates were found in our sample. This finding is striking given the more commonly reported levels of nonadherence found in those being treated for schizophrenia.<sup>6</sup> While we can begin to hypothesize from the current results about which variables may be associated with continuation of an LAI, a more controlled study will allow for more validity and predictive power of the significant findings.

#### Strengths, Limitations, and Directions for Future Research

Strengths. The study assessed adherence without the biases that are often present in formalized clinical trials. Instead, this study looked at adherence within the context of a "real-world" community mental health setting. Research in such a setting does not allow for inflated adherence rates due to monetary reinforcers for study participation and consistent reminder calls. Furthermore, because the majority of patients who come to TRMC have limited financial resources and other socioeconomic stressors, it provides an ideal setting to study adherence in underserved, inner-city populations. Finally, the use of a hazard analysis in the current study allowed for a more in-depth review of the interactions between adherence rates, time, and other variables.

Limitations. The current study provides only a retrospective analysis of a defined timeframe and a nonrandomized population. The findings cannot necessarily be generalized to the wider population of patients being treated with LAIs. The data that were analyzed, while dependable, did not allow for a thorough review of key variables such as relapses, hospitalizations, reasons for missed

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Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration-approved labeling has been presented in this article.

Drug names: aripiprazole (Abilify), haloperidol (Haldol and others), olanzapine (Zyprexa and others), paliperidone palmitate (Sustenna), risperidone (Risperdal and others).

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appointments, reasons for dropout/discontinuations, or patient perceptions of receiving LAIs. Also, some patients who attend higher levels of care do so just until they are stabilized and then return to private providers for continued medication monitoring. Because the current study was archival and did not follow up on patients who were "censored" in the hazard analysis, the results did not account for potential follow through with LAIs at other facilities. Finally, as quantified severity of symptoms and objective accuracy of diagnoses were not considered in the present study, potential impact of these variables on the results cannot be adequately assessed.

Directions for future research. In light of the current findings and limitations of this study, future research looking at variables such as prescriber-patient relationships, prescriber biases about LAIs, the amount and quality of the education on LAIs presented to the patient prior to and upon initiation, acuity of symptoms, and patient reasons for discontinuation will be essential.

Results that indicated the highest level of discontinuation occurred between 16 and 19 months suggest a need for research on the factors arising around this time period that lead to drops in adherence. Future research on adherence may want to use hazard analyses to further assess the interactions between length of time from beginning an LAI and relevant variables.

Finally, while age itself did not have a significant relationship with adherence, age was potentially related to type of LAI prescribed. Understanding these interactions between age and LAI type and even age and length of time on an LAI may help practitioners use different strategies to ensure adherence at each age.

### CONCLUSION

It is crucial that we find ways to support medication adherence for patients with schizophrenia. This study has identified a cohort of highly adherent patients with schizophrenia, receiving a noncoercive, outpatient level of care, being treated with LAIs. It is likely that as the health care system moves to higher-quality, lower-cost solutions, LAIs could play a key role in increasing adherence and decreasing relapses.

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# Posttest

To obtain credit, go to http://www.cmeinstitute.com/activities/Pages/PCC.aspx to complete the Posttest and Evaluation.

- 1. Consistent with previous research, this study found that a patient who is in a partial hospital level of care is more likely to adhere to a long-acting injectable (LAI) antipsychotic in the long-term than is a patient receiving outpatient services.
  - a. True
  - b. False
- 2. According to the results of this study, long-term LAI adherence (from 16 to 23 months) is better with which frequency of therapy?
  - a. Twice a month
  - b. Monthly
- 3. Mr Z is a 20-year-old man who presents to you with schizophrenia and a history of nonadherence to oral antipsychotics because he frequently "forgets" to take them. He is interested in trying an LAI agent. According to the results of this study, which of the following antipsychotics would be the least effective option to improve Mr Z's adherence in the long-term?
  - a. Haloperidol
  - b. Risperidone
  - c. Fluphenazine