Reasons for initiating long-acting antipsychotics in psychiatric practice: findings from the STAR Network Depot Study

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Abstract

Background: Long acting injectable (LAI) antipsychotics have been claimed to ensure treatment adherence and possibly reduce the daily burden of oral formulations. So far, only surveys investigating the theoretical prescribing attitudes of clinicians have been employed. On this basis, we aimed to investigate reasons for prescribing LAIs in a real-world, unselected sample of patients.

Methods: The STAR Network Depot Study is an observational, multicentre study consecutively enrolling adults initiating a LAI over a 12-months period. Clinical severity was assessed with the Brief Psychiatric Rating Scale, and patient's attitude toward medications with the Drug Attitude Inventory 10 items. Psychiatrists recorded reasons for LAI prescribing for each study participant. Responses were grouped into six non-mutually exclusive categories: aggressiveness, patient engagement, ease of drug taking, side-effects, stigma, adherence.

Results: Of the 451 patients included, two-thirds suffered from chronic psychoses. Improving patient engagement with the outpatient psychiatric service was the most common reason for prescribing LAIs (almost 80% of participants), followed by increasing treatment adherence (57%), decreasing aggressiveness (54%), and improving ease of drug taking (52%). After adjusting for confounders, logistic regression analyses showed that reasons for LAI use were associated with LAI choice (e.g. first-generation LAIs for reducing aggressiveness).

Conclusion: Despite the wide availability of novel LAI formulation and the emphasis on their wider use, our data suggest that the main reasons for LAI use have remained substantially unchanged over the years, focusing mostly on improving patient's engagement. Further, clinicians follow implicit prescribing patterns when choosing LAIs, and this may generate hypotheses for future experimental studies.

Keywords: antipsychotic, long-acting injectable, psychiatric practice, prescribing attitudes, survey

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Introduction

Long acting injectable (LAI) antipsychotics were developed with the primary aim of addressing the problem of both hidden and overt non-adherence, which strongly impacts the course and outcome of schizophrenia and related psychoses.[1] Although there is a lack of robust and consistent experimental evidence that LAIs offer better efficacy and tolerability than oral preparations, and that LAI use may increase treatment adherence,[2–4] LAIs provide more reliable drug delivery, reduce peak-trough level differences, and offer greater dosing precision.[1,5] In addition, observational, 'real-world' data have suggested an overall better global outcome

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compared with oral antipsychotics, with a reduced risk of relapse and rehospitalization,[6,7] and possibly a reduction of the burden related to daily medication intake. Although LAIs might be perceived as coercive and stigmatizing by both patients and clinicians, some argued that also the daily administration of oral formulations carries a relevant problem of stigmatization, and that LAIs might even help overcome this issue, if patients are accurately informed and actively involved in the choice of treatment.[1,8–10] Based on these considerations, most international and national guidelines recommended to offer LAIs when poor treatment adherence is a clinical priority and when regular scrutiny of mental health and adverse effects is needed.[11–14] Although data from large observational studies suggest differences in the comparative efficacy of LAIs,[15] guidelines do not provide recommendations on which LAI should be preferred, suggesting to consider the same criteria recommended for the choice of oral antipsychotics.[16] Notably, the indications of LAIs are currently not limited to schizophrenia, but these have also been recommended for management of patients with schizoaffective disorder, delusional disorder, and bipolar disorder.[17]

Despite these recommendations, the rate of LAI use in psychiatric practice is relatively low, leading some experts to argue that LAIs may be under prescribed.[1,2,18–22] As low LAI prescribing may reflect clinician perceptions and attitudes, a number of surveys have been conducted to better understand the reasons for the low prescribing rate of LAIs. Waddell and Taylor, who conducted a systematic review of studies examining attitudes of patients and staff to LAIs, concluded that LAIs continue to have an image problem, exacerbated by the predominant use of these medications as a 'last resort' often for the most stigmatized and chronically ill individuals.[23] Kirschner and colleagues, who recently reviewed patient and clinician attitudes towards LAI antipsychotics in subjects with a first episode of psychosis, confirmed these findings by showing that psychiatrists frequently presume that patients with first-episode psychosis would not accept LAI medications, and that LAIs are mostly eligible for chronic patients.[24] A recent review of barriers for the use of LAIs suggested that many clinicians may presume that patients consider LAIs coercive, and believe that patients taking oral formulations have more control over the management of their illness.[25]

Interestingly, these surveys investigated the theoretical attitudes and beliefs of clinicians, but never assessed the real-world reasons for prescribing LAI medications in unselected samples of everyday patients.[9,26–32] While surveys of attitudes may reflect what clinicians think, and their theoretical knowledge, surveys of patients initiated with LAIs may actually reflect what clinicians do in practice. Hence, the present study investigated the reasons for LAI antipsychotic prescribing in a large cohort of unselected patients starting treatment in Italian psychiatric practice; we additionally sought to determine whether reasons for LAI antipsychotic use had a role in the choice of which LAI antipsychotic was prescribed.

Methods

Study design and inclusion criteria

This study was drawn up following STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) Statement items.[33] The full description of the STAR Network Depot Study methods are reported elsewhere.[34,35] Briefly, the STAR Network Depot Study is an observational, longitudinal, multicentre study involving patients initiating treatment with any LAI, consecutively recruited over a period of 12 months, and assessed after 6 and 12 months of follow-up. Participating centres are inpatient and outpatient services, part of the Italian STAR Network, aimed at gathering original data from real-world clinical practice and providing new pragmatic insights for clinicians and researchers.[36–39] The present paper is focused on baseline data from the recruitment phase.

Patients were included if they were: (a) adults (age $\geqslant$18 years); (b) willing to sign the informed consent; (c) initiating a LAI medication; (d) not receiving any other LAIs during the previous 3 months. Given the pragmatic nature of the study, participants with any psychiatric diagnosis and any concomitant pharmacological treatment were included. Similarly, participants from any setting, including hospital psychiatric wards, community day centres, and residential facilities, were included.

The study protocol was first approved by the Ethics Committee of the coordinating centre [*Azienda Ospedaliera Universitaria Integrata of Verona*; Comitato Etico per la Sperimentazione Clinica (CESC) of the Provinces of Verona and Rovigo, protocol n. 57622 of the 09/12/2015] and was made publicly available at the Open Science Framework online repository (https://osf.io/

wt8kx/). The STAR Network Depot Study was conducted independently of industry funding or support.

Measures

A standard form was used to collect sociodemographic and clinical data. Psychiatrists were also requested to record reasons for LAI prescribing for each study participant. Responses were subsequently grouped into the following six non-mutually exclusive categories: decrease aggressiveness, increase patient engagement (e.g. favouring a closer and more frequent clinical monitoring, possibly increasing attendance to the activities of the outpatient service), improve ease of drug taking, decrease side-effects, decrease stigma, increase adherence to medications. In addition, the following rating scales were used: (i) the clinician-rated Brief Psychiatric Rating Scale (BPRS),[40] which has been validated in the Italian language[41] and showed a high inter-rater reliability in both raters with high and low clinical experience,[42] which assesses the overall level of psychiatric symptoms; (ii) the self-administered Drug Attitude Inventory 10 items (DAI-10),[43] validated in the Italian language,[44] which measures the patient attitude toward medications, with scores ranging between −10 and 10, with higher scores indicating a better overall attitude toward medications; (iii) the clinician-rated Kemp's seven-point scale,[45] compiled by the clinician, which assesses overall adherence to treatments. The scores range from 1 to 7, with higher scores indicating higher levels of adherence. Scores of 5 and above indicate an overall good acceptance of medications. All the staff involved in the recruitment and follow-up of participants took part in a training meeting on the procedures of the study and the use of rating scales.

Data analysis

Continuous variables were expressed as means and standard deviations, while categorical variables were expressed as absolute numbers and percentages. Logistic regression analyses were used to investigate factors associated with LAI choice. The dependent variables were LAI-first generation antipsychotics (FGAs; including haloperidol, fluphenazine, zuclopenthixol, perphenazine) (no = 0, yes = 1), LAI-risperidone (no = 0, yes = 1), LAI-paliperidone (no = 0, yes = 1), LAI-aripiprazole (no = 0, yes = 1), and LAI-olanzapine (no = 0, yes = 1). Independent variables were the following: gender (0 = men, 1 = women); age (years, continuous variable), living conditions (0 = not alone, 1 = alone), educational level (0 = low – up to secondary school, 1 = high – diploma or above), work activity (0 = no, 1 = yes), diagnosis (0 = other, 1 = schizophrenia or related psychoses), substance abuse (0 = no, 1 = yes), length of illness (years, continuous variable), BPRS score (continuous variable), DAI score (continuous variable), Kemp score (continuous variable). The following reasons for LAI use were additionally included into the models: to decrease aggressiveness (0 = no, 1 = yes), to improve patient engagement (0 = no, 1 = yes), to improve ease of drug taking (0 = no, 1 = yes), to decrease side-effects (0 = no, 1 = yes), to decrease stigma (0 = no, 1 = yes), to increase adherence (0 = no, 1 = yes). Regression analyses were based on robust estimator of variance to account for the multicentre observational design.[46] Statistical analyses were performed with the software Stata version 15.1.[47]

Results

Sociodemographic and clinical characteristics

A total of 451 patients initiating treatment with LAI antipsychotics were included in the analysis. Patients were recruited between December 2015 and May 2017. Sixty per cent were males, with a mean age of 42 years. Slightly more than 40% lived alone, and around half had a diploma or a university degree (Table 1). About 22% were employed at the time of recruitment. Two-thirds of the sample suffered from schizophrenia or related psychotic disorders, 18% from bipolar disorder, and the remaining participants from other conditions, including mostly personality disorders and organic mental disorders. We found relatively high rates of alcohol and/or substance abuse (Table 1). Average length of illness was around 12 years, with 50% of the sample being ill for more than 10 years, and only 10% for less than 1 year. The mean BPRS, DAI-10, and Kemp scores are reported in Table 1. Notably, around one-third of patients started treatment with LAI-FGAs, another third with LAI-paliperidone, and one-fourth with LAI-aripiprazole. LAI-risperidone and LAI-olanzapine were the less prescribed LAI formulations (Table 1). For 316 patients (70.1%) this was the first LAI ever prescribed.

Reasons for LAI use

All clinicians reported reasons for prescribing a LAI in each recruited patient. The distribution of

Table 1. Sociodemographic and clinical characteristics of patients initiating treatment with LAI antipsychotics.

	***N*=451**	
	n	**%**
Gender		
Men	274	60.75
Women	177	39.25
Age		
18–30	107	23.94
31–45	161	36.02
36–60	144	32.21
61+	35	7.83
Living conditions		
Alone	195	43.24
Not alone	256	56.76
Educational level		
Up to secondary school	223	50.11
Diploma or above	222	49.89
Work activity		
No	351	77.83
Yes	100	22.17
Diagnosis		
Schizophrenia and related psychosis	325	72.38
Affective disorders	81	18.04
Other	43	9.58
Substance abuse		
No	361	80.04
Yes	90	19.96
Years of illness		
<1	62	13.81
2–5	100	22.27
6–10	74	16.48
11+	213	47.44
BPRS mean score (SD)	48.91	(14.73)

(Continued)

Table 1. (Continued)

	N = 451	
	n	%
DAI-10 mean score (SD)	1.98	(5.34)
Kemp 10-point scale mean score (SD)	4.79	(1.44)
LAI antipsychotic		
FGAs	135	29.93
Risperidone	46	10.20
Paliperidone	139	30.82
Aripiprazole	113	25.06
Olanzapine	18	3.99

BPRS, Brief Psychiatry Rating Scale; DAI-10, Drug Attitude Inventory 10-items; SD, standard deviation.

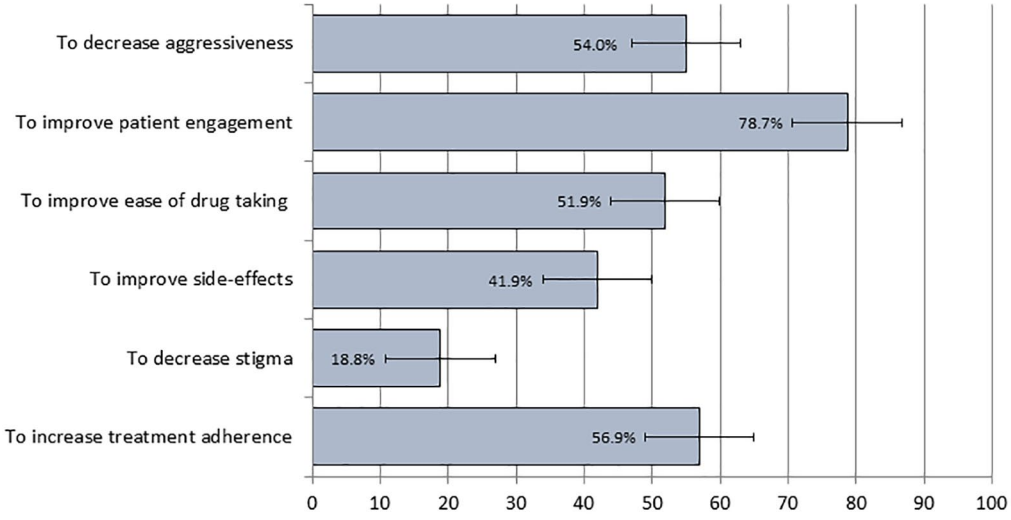

Figure 1. Reasons for long acting injectable antipsychotic use in 451 patients initiating treatment with long-acting antipsychotics.

study participants by reasons for starting treatment with LAI formulations is reported in Figure 1. Improving patient engagement with the outpatient psychiatric service was the most frequently reported reason for LAI use (reported for almost 80% of participants), followed by increasing treatment adherence (57%), decreasing aggressiveness (54%), and improving ease of drug taking (52%). Improving side-effects and decreasing stigma were reasons reported for 42% and slightly less than 20% of study participants (Figure 1). Interestingly, reasons were also associated with LAI choice, as can be seen in Table 2. Decreasing aggressiveness was most often reported in patients who were prescribed FGAs, while improving patient engagement was more often reported in patients who were prescribed risperidone, olanzapine, and FGAs; decreasing stigma was more often reported in patients who were prescribed aripiprazole and olanzapine, while FGAs and olanzapine were more often prescribed for improving treatment adherence (Table 2). Although some prescribers reported that patients were thoroughly informed and actively involved

Table 2. Distribution of reasons for initiating treatment with LAI antipsychotics by type of medication.

	FGAs (*n* = 135)		Risperidone (*n* = 46)		Paliperidone (*n* = 139)		Aripiprazole (*n* = 113)		Olanzapine (*n* = 18)	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
To decrease aggressiveness	96	71.11	19	41.30	73	52.52	51	45.13	9	50.00
To improve patient engagement	111	82.22	41	89.13	105	75.54	83	73.45	15	83.33
To improve ease of drug taking	63	46.67	22	47.83	79	56.83	60	53.10	10	55.56
To improve side-effects	50	37.04	20	43.48	72	51.80	40	35.40	7	38.89
To decrease stigma	21	15.56	8	17.39	25	17.99	27	23.89	4	22.22
To increase adherence	95	70.37	24	52.17	65	46.76	59	52.21	14	77.78

FGA, first generation antipsychotic; LAI, long-acting injectable; *n*, number of patients.

in the choice of initiating a LAI, none indicated an explicit patient preference for LAIs as the main reason for its prescription.

Factors associated with LAI use

Logistic regression analyses were conducted to identify factors associated with LAI use, including whether reasons for LAI prescribing had a role in the choice of which LAI antipsychotic was initiated (Table 3). Among socio-demographic factors, younger age was significantly associated with olanzapine use, higher educational level was associated with aripiprazole use, and unemployment was significantly associated with LAI-FGAs. Among clinical factors, paliperidone was more often prescribed to patients with schizophrenia, while aripiprazole was less often prescribed to patients with schizophrenia. In terms of reasons for LAI prescribing, decreasing aggressiveness was positively associated with LAI-FGAs, but negatively associated with LAI-risperidone and LAI-aripiprazole. LAI-paliperidone was more often prescribed to improve side-effects, and significantly less often prescribed to increase adherence. By contrast, a positive association was found between increasing adherence and use of LAI-olanzapine (Table 3).

Discussion

To our knowledge, this is the first study investigating the reasons for initiating LAI antipsychotics in real-world psychiatric practice. Instead of asking clinicians to report their beliefs and attitudes towards LAIs, which would have elicited general statements potentially not linked to actual LAI prescribing practices, reasons for initiating LAIs in an unselected sample of everyday patients were collected. Likely, this approach may be closer to what clinicians do than to what they think.

A first interesting finding is that LAIs were prescribed to patients with an average length of illness of 12 years, with only 10% being ill for less than 12 months. One-third of patients started treatment with FGAs, one-third with paliperidone, and one-fourth with aripiprazole. Length of illness was not associated with the choice of LAI medications, which suggests not only that these formulations are still mostly used for patients with a long illness history, but also that SGAs were not used in more recent cases as compared with FGAs. The latter finding may be a little surprising in view of experts and international clinical guidelines advocating for an earlier and broader use of LAIs, especially SGAs.[1,48]

Reasons for LAI prescribing may help understand this pattern of drug use. Aspects related to the burden of side-effects or to the stigma associated with some LAI medications were not reported as the most common reasons for LAI prescribing. By contrast, LAIs were most frequently prescribed to keep the patients engaged with the psychiatric service, to optimize treatment adherence, and also to reduce aggressiveness. Overall, these reasons may reflect a quite conventional use of LAIs rather than a cultural change with LAIs being used as an alternative to oral medications in patients expressing a preference for such a formulation. It should be recognized, however, that expert guidelines emphasize that LAI formulations provide an opportunity

Table 3. Factors associated with LAI antipsychotic choice: logistic regression analyses.

	Variable	FGAs OR (95% CI)	Risperidone OR (95% CI)	Paliperidone OR (95% CI)	Aripiprazole OR (95% CI)	Olanzapine OR (95% CI)
Sociodemographic	Gender, 0 = men, 1 = women	1.12 (0.69–1.82)	0.63 (0.30–1.30)	0.97 (0.57–1.65)	1.02 (0.60–1.74)	1.13 (0.28–4.49)
	Age, years	1.02 (0.99–1.04)	1.02 (0.99–1.06)	0.98 (0.96–1.01)	0.98 (0.96–1.01)	**0.94 (0.90–0.99)**
	Living conditions, 0 = not alone, 1 = alone	1.43 (0.75–2.69)	0.56 (0.26–1.23)	0.82 (0.49–1.40)	0.96 (0.55–1.67)	1.49 (0.42–5.29)
	Educational level, 0 = low, 1 = high	0.76 (0.46–1.25)	0.90 (0.45–1.80)	0.77 (0.48–1.26)	**2.20 (1.31–3.69)**	0.61 (0.22–1.65)
	Work activity, 0 = no, 1 = yes	**0.53 (0.30–0.93)**	1.73 (0.78–3.80)	1.44 (0.85–2.41)	1.11 (0.66–1.86)	0.41 (0.08–2.11)
Clinical	Diagnosis, 0 = other, 1 = schizophrenia	0.92 (0.57–1.49)	0.77 (0.37–1.59)	**2.01 (1.16–3.48)**	**0.55 (0.34–0.87)**	2.13 (0.51–8.87)
	Substance abuse, 0 = no, 1 = yes	1.48 (0.82–2.65)	1.16 (0.44–3.00)	1.20 (0.71–2.03)	0.60 (0.28–1.28)	0.51 (0.11–2.27)
	Length of illness, years	1.02 (0.99–1.05)	0.98 (0.94–1.03)	1.00 (0.97–1.02)	0.97 (0.95–1.01)	0.98 (0.90–1.06)
	BPRS, continuous variable	**0.98 (0.96–0.99)**	1.02 (0.99–1.04)	**1.02 (1.01–1.04)**	0.99 (0.97–1.01)	**0.96 (0.93–0.99)**
	DAI-10, continuous variable	0.95 (0.90–1.01)	1.01 (0.95–1.07)	0.99 (0.94–1.04)	1.04 (0.98–1.11)	1.00 (0.90–1.12)
	Kemp 10-point scale, continuous variable	0.91 (0.72–1.14)	0.82 (0.62–1.08)	1.19 (0.96–1.49)	1.08 (0.85–1.36)	0.70 (0.45–1.07)
Reasons for LAI use	To decrease aggressiveness, 0 = no, 1 = yes	**2.79 (1.69–4.62)**	**0.45 (0.22–0.93)**	0.86 (0.53–1.40)	**0.63 (0.40–0.98)**	0.57 (0.19–1.65)
	To improve patient engagement, 0 = no, 1 = yes	1.06 (0.55–2.04)	2.40 (0.67–8.59)	0.66 (0.36–1.22)	0.98 (0.58–1.65)	1.43 (0.37–5.54)
	To improve ease of drug taking, 0 = no, 1 = yes	1.08 (0.66–1.77)	0.87 (0.41–1.84)	0.96 (0.60–1.53)	0.87 (0.52–1.48)	1.46 (0.44–4.81)
	To improve side-effects, 0 = no, 1 = yes	0.74 (0.47–1.16)	1.12 (0.55–2.27)	**1.77 (1.14–2.75)**	0.65 (0.40–1.07)	0.91 (0.31–2.63)
	To decrease stigma, 0 = no, 1 = yes	1.12 (0.54–2.31)	0.91 (0.35–2.36)	0.68 (0.36–1.27)	1.34 (0.72–2.48)	1.47 (0.37–5.90)
	To increase adherence, 0 = no, 1 = yes	1.71 (0.96–3.06)	0.60 (0.29–1.23)	**0.56 (0.35–0.87)**	1.11 (0.59–2.09)	**3.76 (1.01–14.36)**

BPRS, Brief Psychiatry Rating Scale; CI, confidence intervals; DAI-10, Drug Attitude Inventory 10-items; FGA, first-generation antipsychotic; LAI, long-acting injectable; OR, odds ratio.

for regular scrutiny of a patient's mental state and adverse effects by the health-care professional administering the injection, and that they assure awareness of compliance.[11–14] We argue that these arguments are in line with the two most commonly reported reasons for prescribing, namely service engagement and treatment adherence.

The present analysis showed that reasons for LAI use had a role in the decision of which LAI was prescribed. This finding is new and clinically interesting as it provides some insights into the clinicians' prescribing decisional process. Logistic regression analyses suggested that some clinical presentations were more or less likely to be treated with individual LAIs: for example, aggressiveness was positively associated with FGA prescribing, but negatively associated with use of aripiprazole or risperidone. This is in line with pharmacoepidemiological surveys of LAI use. For example, Tang and colleagues, who described use of FGA and SGA LAI drugs and their clinical correlates among 3557 subjects diagnosed with schizophrenia across 15 Asian countries, found that being prescribed a FGA *versus* a SGA LAI was associated with aggression and disorganization.[49] The notion that LAI formulations, and FGA LAIs in particular, may be particularly beneficial in psychotic patients with violent behaviour, is corroborated by evidence showing that LAI formulations significantly reduce the severity of hostility, aggressiveness, number of violent incidents, and criminal offence.[50] Consistently with this notion, which has been particularly emphasized for FGAs, Italian psychiatrists tended to prefer FGA-LAIs in the case of aggressiveness.

The need for improving adherence was positively associated with use of olanzapine and negatively associated with use of paliperidone. As there are no experimental data suggesting lower discontinuation rates for olanzapine over alternative LAI formulations in poorly adherent patients, this pattern of drug use may reflect the practicalities of olanzapine LAI, especially the need for post-injection monitoring in a healthcare facility where access to appropriate medical care in the case of overdose can be assured. It is therefore possible that the choice of olanzapine in participants with poor treatment adherence offered an opportunity for patient closer scrutiny by mental health professionals, aiming to increase engagement with the psychiatric facility, and adherence in the long-term. This pattern of olanzapine LAI use may imply that prescribers may be inclined to expose patients to a risk of post-injection syndrome and to a resource intensive monitoring in particularly difficult-to-treat patients, with important adherence problems and, possibly, with a particularly severe illness course.

Other interesting patterns of LAI prescribing included a more frequent use of aripiprazole, rather than other LAIs, in patients without a diagnosis of schizophrenia and related psychosis and in those with higher educational level, while the contrary was true for paliperidone, more often chosen in people with schizophrenia and related psychosis. Likely, this pattern of drug use is a reflection of the licensed indications of these medications as, currently, in Italy, aripiprazole, but not paliperidone, holds a marketing authorization for use in people with bipolar disorder. Interestingly, not only was paliperidone the most prescribed LAI, but also the only LAI that clinicians prescribed aiming to decrease the burden of side-effects. As experimental data suggested that paliperidone substantially equals olanzapine and risperidone in terms of metabolic effects and prolactin level increase,[51] its popularity may likely be related to its enhanced practicality compared with the biweekly administration of risperidone-LAI, and to the complex regulatory requirements of olanzapine-LAI. Surprisingly, aripiprazole-LAI was not commonly prescribed with the primary intent of reducing the burden of side-effects, although it has a favourable tolerability profile in terms of metabolic side-effect and hyperprolactineamia.[51]

This study has important limitations. First, the cross-sectional design employed cannot detect causal associations between variables, and all statistical associations discussed should be regarded as merely exploratory and hypothesis-generating. Second, the use of simple rating scales (in accordance to the pragmatic attitude of the study) might have affected the precision in measuring some important dimensions, such as psychiatric symptoms and patients' attitudes toward medications. Third, characteristics of recruiting centres were heterogeneous in terms of settings (e.g. community services, hospital wards, rehabilitation facilities), and each site contributed to the recruitment to a different extent. Fourth, various local factors may have strongly influenced prescribing attitudes of each centre (e.g. local guidelines and long-standing habits, availability of medications). This, along with our wide inclusion criteria, led to heterogeneity in the recruited population. Although this reflects the complexity of real-world clinical

settings, bolstering the external validity of results, it may at the same time affect internal validity. To address this limitation, we employed statistical techniques accounting for variability between centres. Finally, we were not able to compare patients initiating a LAI with those who did not, under similar clinical circumstances. Future studies might aim to include this comparison, in order to clearly detect which elements are crucial in the decision of starting LAI formulations.

In conclusion, analysis of the reasons for LAI antipsychotic drug prescribing in a large cohort of unselected patients documented that LAI formulations are mostly used in people with irregular contacts with the outpatient psychiatric services and, more generally, in people with poor treatment adherence. These findings suggest that the main reasons for LAI use have remained substantially unchanged over the years, despite the availability of SGAs as LAI formulations have suggested a wider and earlier use of these formulations.[48,52] Very importantly, reasons for LAI prescribing influenced the choice of which LAI antipsychotic was prescribed, thus suggesting that in clinical practice clinicians may have implicit prescribing patterns leading to the use of different LAI formulations based on different clinical needs. This aspect is of paramount relevance as it may be used to generate new research hypotheses on potential differences among LAI medications to be tested by means of pragmatic experimental studies.

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