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Attitude and perceptions of patients towards long acting depot injections (LAIs)

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ABSTRACT

Background: Despite the well-established efficacy of the long acting depot injectable (LAIs) antipsychotics, these are significantly underused and underutilized by the mental health professionals, with a belief that patients will not accept the same.

Aims & objectives: To explore the acceptability and perception of patients towards various psychiatric treatments, with specific focus on LAIs. Additionally the study aimed to compare the acceptability of various types of treatments including LAIs between patients with severe mental disorders (Psychotic disorders and Bipolar disorder) and those with Common mental disorders (Anxiety, neurotic and depressive disorders).

Methodology: A self-designed semi-structured questionnaire was used to evaluate the preferred treatment options of all the new patients attending the psychiatry outpatient clinic of a tertiary care hospital. Depending on the response, they were further probed for the reasons for accepting or rejecting the LAIs.

Results: 2659 patients were interviewed who were divided into two groups (Group I - 321 subjects with psychotic disorders and 120 subjects with bipolar affective disorder (BPAD) and Group II – 2218 subjects with neurotic, stress-related and unipolar depressive disorders). More than three-fourth (78.8%) of the participants in the whole study sample opted for tablets only as their first preferred choice and injectables were opted by about 5% of the participants only, with no significant difference between the 2 groups. After being explained about LAIs, one fourth of the participants (24.9%) reported that they may consider LAIs, without any significant difference between the 2 groups. Among those who refused to take LAIs even after explanation, the commonly reported reasons were difficulty in visiting hospital frequently for the injectables (41.69%), injectables being painful (19.41%), fear of injections (13.96%), no need to take LAIs (12.45%) and preference to take some other types of medicines (8.52%).

Conclusions: Considering the fact that LAIs are highly underused in patients with severe mental disorders and there is lack of awareness about LAIs among patients with severe mental disorders, the present study findings suggest that there is reasonable level of acceptance of LAIs among patients with severe mental disorders when explained about the same.

1. Introduction

Medication non-adherence is a common problem in medical practice across different specialties (Hugtenburg et al., 2013; Marcum et al., 2013). In general it is reported that about half of the patients with various psychiatric disorders do not adhere to their medications (Nosé et al., 2003; Velligan et al., 2009). Poor adherence has been strongly associated with higher risk of relapse, increased hospitalization rates, lower rates of remission of positive symptoms and poorer quality of life (Coldham et al., 2002; Lingam and Scott, 2002; Malla et al., 2002; Velligan et al., 2010a).

To overcome the problem of treatment non-adherence, over the years long acting injectables (LAI), sustained release formulations, implants and transdermal patches have been developed (Chapman and Horne, 2013; Haddad et al., 2014; Velligan et al., 2010b). These formulations provide the required dose of medications over the period of time and resultantly patients are not required to take the oral formulations daily (Dufort and Zipursky, 2019; Haddad et al., 2014). Apart from addressing the medication non-adherence, evidence also suggests that LAIs help in achieving remission and maintaining remission for

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longer duration (Giraud-Baro et al., 2016; Llorca et al., 2008), reducing relapse rates and frequent hospitalizations (Leucht et al., 2011) and improved health-related quality of life in patients with schizophrenia (Nasrallah et al., 2004).

Although, antipsychotics are used primarily for management of psychotic disorders, but these are also used for management of various other psychiatric disorders, such as bipolar disorder, depressive disorders, obsessive compulsive disorder etc (El-Khayat and Baldwin, 1998; Goodnick and Barrios, 2001; Veale et al., 2014; Yatham et al., 2005). Among the various types of long acting formulations, few antipsychotic LAIs are being marketed and have been reported to be associated with lower risk of relapse and improved outcome among patients with psychotic disorders and bipolar disorder (Brissos et al., 2014; Llorca et al., 2013). Despite this in general there are low prescription rates of LAIs in routine clinical practice (Ahn et al., 2008; Fayek et al., 2003). Low prescription rates of LAIs have been linked to the attitudes of psychiatrists and patients towards the same (Heres et al., 2007, 2006; Kim et al., 2012; Patel et al., 2009; Samalin et al., 2013). Evidence suggests that usage of LAIs after the introduction of second-generation (atypical) oral antipsychotics have been mostly limited to those with poor adherence, poor insight and history of aggression (Malla et al., 2013, 2002; Manchanda et al., 2013; Stevens et al., 2016).

Studies which have evaluated the attitudes of mental health professionals and psychiatric nurses towards antipsychotic LAIs suggest that there is wide variation in the attitude of the mental health professionals to the use of antipsychotic LAIs and offering the same to the patients, who may benefit from the same (Waddell and Taylor, 2009). There is a common notion among the psychiatrists' that patients would not accept antipsychotic LAIs (Heres et al., 2006; Iyer et al., 2013a; Manchanda et al., 2013).

Compared to the data on the attitudes of mental health professionals and psychiatric nurses towards antipsychotic LAIs, there is limited data on the patient's preference and acceptability for antipsychotic LAIs (Iyer et al., 2013b; Walburn et al., 2001). Further, the studies which have evaluated the same have been mostly limited to those who are already on LAI antipsychotics (Caroli et al., 2011). A systematic review of 6 studies which explored the patient satisfaction and preference for LAI antipsychotics suggest that there is high acceptability and preference for LAI antipsychotic over oral antipsychotic medications in those already receiving LAI antipsychotic (Hoencamp et al., 1995; Larsen and Gerlach, 1996; Pereira and Pinto, 1997; Walburn et al., 2001; Warren, 1998). Some of the studies which have compared the patients receiving and not receiving LAI antipsychotic suggest that, the acceptance rate of depot-naïve patients are significantly lower than those already on LAI antipsychotic (Heres et al., 2007). Data also suggests that patients receiving an LAI antipsychotic often report embarrassment or shame, stigma and perception of coercion with the use of antipsychotic LAI antipsychotic, which cannot be undermined (Patel et al., 2009, 2008). Evidence also suggest lack of awareness and knowledge about LAI antipsychotic among the patients, with some of the patients reporting of never heard about LAI antipsychotic, others had not understood when LAI antipsychotic were discussed with them and those who had heard about LAI antipsychotic had notion in the context of coercion or medication non-adherence (Iyer et al., 2013b).

Since 2002, second generation antipsychotic LAI preparations have been available in the market with better side-effect profile compared to first generation antipsychotic LAIs (Fleischhacker et al., 2003; Miyamoto and Wolfgang Fleischhacker, 2017), yet the prescription rates of LAI antipsychotic had not increased substantially. Surveys of psychiatrists' across the world suggest that there is an anticipated negative attitude of the patients towards LAI antipsychotics which prevent them from offering the same (Heres et al., 2006; Iyer et al., 2013a; Patel et al., 2003). Studies reporting high acceptance rates for LAI antipsychotics among patients with schizophrenia are limited to the opinions of the participants attending depot clinics in Western countries, resultantly such data cannot be considered as representative of the community/hospital attending patients population (Walburn et al., 2001). There is no data from developing countries like India, with respect to the attitude of patients with various psychiatric disorders towards LAIs. In this background, the present study was designed to explore about the acceptability and perception of patients towards various psychiatric treatments, with specific focus on LAIs. Additional aims were to compare the acceptability of various types of treatment between patients with severe mental disorders (Psychotic disorders and Bipolar disorder) and those with common mental disorders (Anxiety, neurotic and depressive disorders). Further an attempt was made to evaluate whether the history of poor compliance in the past influences the acceptability of LAIs in patients with various psychiatric disorders.

2. Methodology

A cross-sectional study design was used in which a self-designed questionnaire was used to evaluate the preferred treatment options of all the new patients attending the psychiatry outpatient clinic of a tertiary care hospital before they met the treating clinician.

In our setup, new subjects/patients have to get registered with our Out-patient department (OPD) clinic before visiting the treating psychiatrists. For this study, the newly registered subjects were initially interviewed by qualified psychiatrists (study authors) for their presenting complaints before they visited their treating psychiatrists (unrelated to the study) and were initially asked about their treatment history and then asked about their preferred treatment options. When the initial preference was evaluated, the patients were asked to report the kind of treatment, they would prefer, without asking them about any specific treatment. In case, patient reported preference for injectables, they were asked about kind of injectables they were aware of. Then they were provided information about LAIs, i.e., for certain psychiatric conditions, treatment formulations in the form of intramuscular injectables are available, which can be used once or twice a month, instead of daily intake of medications. They were also explained that these injectables have additional benefits in the form of no need to take the medication daily and resultant improvement in medication compliance, reduction in psychopathology, lesser chance of relapse of symptoms, more chances of symptom amelioration, and remaining in clinical remission for longer duration. After providing this information the patients were asked, whether they would prefer to take the same or not. Depending on the response, they were further probed for the reasons for accepting or rejecting the LAIs.

The study was carried out during the period from January- April 2016.To be included in the study, the patients were required to be aged at least 18 years and diagnosed with a primary psychiatric disorder as per the ICD-10 criteria based on the interview by a trained psychiatrist. Those who were diagnosed with intellectual disability, dementia, delirium or only personality disorders and uncooperative were excluded. Written informed consent was obtained from all the study participants, before being enrolled into the study and the study was approved by the Institute Ethics Committee.

To understand the impact of diagnosis, the study sample was categorized into 2 groups, based on the need of use of antipsychotics for long duration. Patients with psychotic and bipolar disorder group were combined into one group (Group-I) and they were compared with those with Neurotic and stress related group, including those with depressive disorders (Group-II).

The data obtained was analyzed by using SPSS-14. Frequency and percentages were calculated for the categorical variables and mean and standard deviations were calculated for continuous variables. Comparisons were done by using Chi-Square test and t-test.

3. Results

The study sample comprised of 2659 patients, with males outnumbering the females. Majority of the participants were married, not

Table 1
Socio demographic comparison of the two groups.

Variables	Whole sample (n = 2659)	Psychosis group (n = 321)	BPAD (n = 120)	Neurotic, stress related disorders and depressive disorders (n = 2218)	Comparison of Psychotic and Bipolar disorder group	Comparison of Psychotic + Bipolar disorder group with Neurotic, stress related disorders and depressive disorders
		Mean (SD)/ Frequency (%)	Mean (SD)/ Frequency (%)	Mean (SD)/ Frequency (%)	Chi-square/t-test (p-value)	Chi-square/t-test (p-value)
Age (in yrs)	38.22 (14.94)	38.21 (14.09)	37.51 (15.33)	38.25 (15.04)	0.451 (0.652)	−0.306 (0.759)
Gender						
Male	1476 (55.5%)	174(54.2%)	73 (60.8%)	1229 (55.5%)	1.557 (0.212)	0.053 (0.817)
Female	1183 (44.5%)	147 (45.8%)	47 (39.2%)	989 (44.6%)		
Marital status						
Married	1811 (68.1%)	223 (69.47%)	81 (67.5%)	1507 (67.9%)	0.158 (0.691)	0.166 (0.684)
Unmarried	848 (31.9%)	98 (30.52%)	39 (32.5%)	711 (32.1%)		
Occupation						
Employed	968 (36.4%)	58 (18.06%)	53 (44.16%)	857 (38.6%)	**31.587(< 0.001)*** **	**28.822(< 0.001)*** **
Unemployed	1691 (63.8%)	263(81.93%)	67 (55.83%)	1361 (61.4%)		
Years of Education	10.81(5.29)	10.85 (4.90)	10.30 (5.23)	10.83 (5.35)	1.035 (0.301)	−0.477(0.655)
Religion						
Hindu	1770 (66.6%)	239(74.45%)	78 (65%)	1453 (65.5%)	**3.863(0.049)***	**6.712(0.010)****
Non-Hindu	889 (33.4%)	82(25.54%)	42 (35%)	765 (34.5%)		
Family type						
Nuclear	1417 (53.3%)	197(61.37%)	58 (48.33%)	1162 (52.4%)	**6.088 (0.014)***	**4.363(0.037)***
Non-nuclear	1242 (46.7%)	124 (38.63%)	62 (51.66%)	1056 (47.6%)		
Locality						
Rural	1195 (44.9%)	148 (46.10%)	51 (42.5%)	996 (44.9%)	0.459(0.498)	0.007(0.933)
Urban	1464 (55.1%)	173 (53.89%)	69 (57.5%)	1222 (55.1%)		

on paid job, Hindu by religion and from nuclear families. Those from urban localities outnumbered those from rural localities. Majority of the participants were diagnosed with neurotic spectrum disorders or depressive disorders (Table 1). Slightly more than one-tenth of the study sample comprised of those with diagnosis of psychotic spectrum (mostly schizophrenia) and slightly less than 5% were diagnosed with bipolar disorder. When the patients with psychotic disorders and bipolar disorder were compared for their sociodemographic profile, significant differences were seen only in the areas of employment status and religion, with significantly higher proportion of those with psychotic disorders being unemployed and belonging to Hindu religion.

When patients with psychotic and bipolar disorder group (Group-I) were compared with those with Neurotic and stress related group, including those with depressive disorders (Group-II), statistically significant differences were seen for the variables of employment, religion and family type with significantly higher proportion of patients in Group-I being unemployed, Hindu by religion and belonging to nuclear families (Table 1).

4. Comparison of preferred treatment between those with Psychotic + Bipolar disorder group (Group-I) and those with Neurotic, stress related disorders and depressive disorders (Group-II)

The mean duration of illness was significantly longer for Group-I, when compared with the Group-II.About half of the participants were taking some psychiatric treatment prior to the current consultation, which was significantly higher for the patients belonging to Group-I. Among, those who had received some form of psychiatric treatment in the past, it was mostly in the form of tablets. When both the groups were compared for specific types of treatments received in the past, significantly higher proportion of those in group-I were on tablets and injectables, while significantly higher proportion of those in group II received capsules or had not received any treatment.

Medication non-adherence as defined as life time history of one episode of non-adherence to medications for at least one month in the whole study sample was 40.4% (n = 1075). However, when the same was evaluated among those who had received treatment with any psychotropics (not necessarily LAIs) was about 90% (1054 of 1171); this was more in psychotic and BPAD group (97.2%), when compared to the neurotic, stress related and depressive disorder group (88.4%) and the difference between the two groups was statistically significant.

When the patients were asked regarding their preferred treatment (they had the option of reporting more than one treatment), majority of them opted for tablets and this was followed by capsules (Table 2). When both the groups were compared, significantly higher proportion of patients in group-I opted for injectables, whereas significantly higher proportion of those in group-II opted for tablets only or had no specific preference. When asked further about the first preferred treatment, more than three-fourth (78.8%) of the participants in the whole study sample opted for tablets only. LAIs were opted by about 5% of the participants only, with no significant difference between the 2 groups. In terms of second and third preferred treatment, only about one-tenth (10.4%) and about 6.13% of them opted for LAIs respectively, with no significant difference between the 2 groups. When specifically asked about LAIs after being provided information about the same, only one fourth of the participants (24.9%) reported that they may consider LAIs, without any significant difference between the 2 groups. Those who opted for LAIs, when asked about why they would prefer the same, only 7.7% of them reported problem with taking medicines as a reason and more than four-fifth of them, did not give any specific reason for the same. Those who refused to take LAIs, when asked for reasons for the same, two-fifth of them (41.69%) reported that it is difficult to visit the hospital frequently for the injectables. Other common reasons reported for not preferring LAIs included injectables being painful (19.41%), fear of injections (13.96%), there is no need to take LAIs (12.45%) and because they would prefer to take some other types of medicines (8.52%) (Table 2).

4.1. Comparison of psychotic and bipolar disorder group

When similar comparisons were made between psychotic and bipolar disorder group, it was found that all the patients with psychotic disorders with past history of treatment (n = 157) had lifetime history

Table 2
Comparison of preferred treatment between those with Psychotic + Bipolar disorder group (Group-I) and those with Neurotic, stress related disorders and depressive disorders.

Variables	Whole Group (n = 2659) Mean (SD)/ Frequency (%)	Psychosis group + BPAD (n = 441) Mean (SD)/ Frequency (%)	Neurotic, stress related disorders and depressive disorders (n = 2218) Mean (SD)/ Frequency (%)	Chi-square/Mann-Whitney(p-value)
Duration of illness in months	36.80 (50.60)	50.38 (63.81)	34.09 (47.09)	**U = 409305.0 (< 0.001)*****
Lifetime history of at least 1 episode of poor medication adherence (n = 2659)	1075 (40.4%)	212 (48.1%)	863 (38.9%)	**12.82 (< 0.001)*****
Lifetime history of at least 1 episode of poor medication adherence in those who had previous history of receiving psychotropic treatment (n = 1171)	**1054 (90.0%) (n = 1171)**	**207 (97.2%) (n = 213)**	**847 (88.4%) (n = 958)**	**14.902(< 0.001)*****
Past Psychiatric treatment				
Psychotherapy/counselling only	20 (0.8%)	2 (0.5%)	18 (0.8%)	0.63 (0.427)
Medication + Counselling	61 (2.3%)	5 (1.1%)	56 (2.5%)	3.175(0.075)
Tablets only	995 (37.4%)	**191 (43.3%)**	804 (36.2%)	**7.834 (0.005)****
Capsules only	62 (2.3%)	**1 (0.2%)**	61 (2.8%)	**10.286 (< 0.001)*****
Injectables/LAI only	27 (1.0%)	**13 (2.9%)**	14 (0.6%)	**19.642 (< 0.001)*****
Combination of LAI and tablets	6 (0.2%)	1 (0.2%)	5 (0.2%)	0.001 (0.995)Y
No current treatment	1488(56.0%)	228 (51.70%)	**1260 (56.80%)**	**3.893 (0.048)***
Preferred treatment (Multiple answers)				
Psychotherapy/counselling only	307 (11.5%)	53 (12.0%)	254 (11.5%)	0.116 (0.734)
Medication + Counselling	115 (4.3%)	21 (4.8%)	94 (4.2%)	0.244 (0.621)
Tablets only	1352(50.8%)	200 (45.4%)	**1152 (51.9%)**	**6.387 (0.011)***
Capsules only	324(12.2%)	54 (12.24%)	270 (12.2%)	0.002(0.966)
Injectables/LAI only	83(3.1%)	**56 (12.7%)**	27 (1.2%)	**160.34(< 0.001)*****
Electroconvulsive therapy (ECT)	41(1.5%)	10 (2.3%)	31 (1.4%)	1.834 (0.176)
Combination of tablets and capsules	52 (2.0%)	13 (2.9%)	39 (1.8%)	2.715 (0.099)
Combination of LAI and tablets/capsules	39(1.5%)	8 (1.81%)	31 (1.4%)	0.441 (0.506)
Medication and ECT	35(1.3%)	5 (1.13%)	30 (1.4%)	0.136 (0.713)
No specific preference	305(11.47%)	**16 (3.6%)**	**289 (13.0%)**	**32.02 (< 0.001)*****
Type of preferred treatment -First preference				
Psychotherapy/counselling only	275(10.3%)	42 (9.5%)	233 (10.5%)	0.38 (0.536)
Medication + Counselling	26 (1.0%)	6 (1.4%)	20 (0.9%)	0.79 (0.37)
Tablets only	**2096(78.8%)**	345 (78.2%)	1751 (78.9%)	0.11 (0.737)
Capsules only	**21 (0.8%)**	3 (0.7%)	18 (0.8%)	0.08 (0.77)
Injectables/LAI only	**129 (4.9%)**	**24 (5.4%)**	**105 (4.7%)**	0.399(0.527)
ECT	1 (0.03%)	1 (0.2%)	0 (0%)	-
No preference – Left to doctor to decide	111 (4.2%)	20 (4.5%)	91 (4.1%)	0.171(0.678)
Second preference				
Psychotherapy/counselling only	8 (0.3%)	1 (0.2%)	7 (0.3%)	0.09(0.755)
Medication + Counselling	9 (0.3%)	0 (0%)	9 (0.4%)	-
Tablets only	63 (2.4%)	13 (2.9%)	50 (2.3%)	0.765(0.381)
Capsules only	**221 (8.3%)**	40 (9.1%)	181 (8.2%)	0.399 (0.527)
Injectables/LAI only	**277 (10.4%)**	43 (9.8%)	234 (10.6%)	0.25 (0.615)
Combination of LAI and tablets	1(0.037%)	0 (0%)	1 (0.04%)	-
No second preference – left to doctor	2080(78.2%)	344 (78.0%)	1736 (78.3%)	0.015(0.902)
Third preference				
Psychotherapy/counselling only	2 (0.075%)	0 (0%)	2 (0.1%)	-
Tablets only	3 (0.112%)	1 (0.2%)	2 (0.1%)	0.609 (0.435)Y
Capsules only	7 (0.263%)	1 (0.2%)	6 (0.3%)	0.02 (0.869)
Injectables/LAI only	**163 (6.13%)**	**32 (7.3%)**	131 (5.9%)	1.16 (0.280)
Combination of tablets and capsules	3 (0.112%)	1 (0.2%)	2 (0.1%)	0.60 (0.434)Y
Combination of LAI and tablets	1 (0.037%)	**0(0%)**	1 (0.04%)	-
No third preference – left to doctor	2480 (93.3%)	406 (92.1%)	2074 (93.5%)	1.22 (0.268)
Will you prefer to take LAIs?				
Yes	662 (24.9%)	103 (23.4%)	559 (25.2%)	0.750 (0.687)
No	1854 (69.7%)	315 (71.4%)	1539 (69.4%)	
Did not reply	143 (5.4%)	23 (5.2%)	120 (5.4%)	
Reasons for preference for LAIs - if yes	(N = 662)	(N = 103)	(N = 559)	
No problem in taking it	13 (1.96%)	3 (2.91%)	10 (1.78%)	0.57 (0.45)
Problem with medicine	51 (7.70%)	11 (10.67%)	40 (7.15%)	1.51 (0.217)
Easy	9 (1.35%)	3 (2.91%)	6 (1.07%)	2.19 (0.138)
Long acting – have to take once in few days	36 (5.43%)	2 (1.94%)	34 (6.08%)	2.89 (0.088)
Less side effects than medicines	2 (0.302%)	0 (0%)	2 (0.35%)	-
No specific reason	551 (83.23%)	84 (81.5%)	467(83.54%)	0.24 (0.619)
Reason for not preferring LAIs	(N = 1854)	(n = 315)	(n = 1539)	
No need	231 (12.45%)	31 (9.84%)	200 (12.99%)	2.38 (0.122)
Difficulty to go to hospital to take injections	773 (41.69%)	119 (37.77%)	654 (42.49%)	2.39 (0.121)
Uncomfortable with injection	21 (1.13%)	4 (1.26%)	17 (1.10%)	0.0016 (0.968)
Pain	360 (19.41%)	66 (20.95%)	294 (19.10%)	0.57 (0.449)
Prefer other type of medicines	158 (8.52%)	30 (9.52%)	128 (8.31%)	0.488 (0.484)

(*continued on next page*)

Table 2 (*continued*)

Variables	Whole Group (n = 2659) Mean (SD)/ Frequency (%)	Psychosis group + BPAD (n = 441) Mean (SD)/ Frequency (%)	Neurotic, stress related disorders and depressive disorders (n = 2218) Mean (SD)/ Frequency (%)	Chi-square/Mann-Whitney(p-value)
Fear of injection	259 (13.96%)	47 (14.92%)	223 (14.48%)	0.039 (0.843)
No specific reason	41 (2.21%)	18 (5.71%)	23 (1.49%)	21.53 (< 0.001)***

Y-Chi Square value with Yate's correction.

of at least 1 episode of medication non-adherence as compared to those with bipolar disorder with history of past treatment history [N = 157 (100%) versus 50 (89.3%); Chi-square test-17.309; p value < 0.001***]. No significant differences emerged for any other variables between the psychotic and bipolar disorder group (Table 3).

4.2. Comparison of patients with and without past psychiatric treatment history

When those who had received psychiatric treatment in the past and those who had not received the psychiatric treatment in the past were compared, those who had received treatment in the past significantly more often reported preference for combination of medication and psychotherapy [89 (7.60%) vs 26 (1.77%); Chi-square – 54.253; p-value < 0.001***], capsules only [164 (14.0%) Vs 160 (10.75%); Chi-square – 6.478; p-value −0.011*] and expressed no specific preference [169 (14.43%) Vs 136 (9.13%); Chi-square −18.074;p-value − < 0.001***].

Though no significant differences were noted with regard to first, second and third preferences but most common first preference of patients who had received treatment in the past was tablets only (1187;79.77%), followed by counselling only (158;10.61%) and injectables/LAIs (69;4.83%); second common preference was injectables/LAIs (168;11.29%) followed by capsules only (118;7.93%) and third common preference was LAIs (89;5.98%). While 23.5% of patients who had received treatment in the past reported they would agree for LAIs, 72.04% refused for LAIs and about 4.36% did not reply for LAIs option. A slightly higher number of patients who had received psychiatric treatment in the past agreed for LAIs when compared to those who had not received any treatment (311; 26.55%). No significant differences were noted in reasons for preference or non-preference for LAIs in these two groups of patients.

When the preference for LAIs was evaluated specifically among those who had received treatment with any psychotropics in the past (N = 1171) and had history of non-adherence (N = 1054), it was seen that they had significantly lower preference for LAIs (23.5% versus 58.11%; Chi-square value 66.41; p value < 0.001***).

5. Discussion

The present study explored the acceptability and perception of patients towards various psychiatric treatments, with specific focus on LAIs. As there is no specific questionnaire to assess the treatment acceptability, a short, simple questionnaire was designed for this study. The patient population examined in this study was broad and included patients with severe mental illness (SMI) and those with common mental disorders. Even though no specific LAIs are currently used for the second group of patients (neurotic, stress related disorders and depressive disorders), yet an attempt was made to explore the acceptability of LAIs among patients with all kind of psychiatric illness. This was also done to have a comparison group, against which the acceptability of LAIs among patients with SMI could be compared.

The demographic profile of the patients included in the present study was typical of patient population attending the walk-in clinic of our centre (Grover et al., 2012), suggesting that the patient population included in the present study was fairly representative.

With regard to the past psychiatric treatment at the time of assessment, it was seen that in those who had past psychiatric treatment history, almost all the patients had received some form of oral medications with only 1.0% of the patients receiving antipsychotic LAIs and 0.2% of patients receiving a combination of oral medication and an LAI antipsychotic medication. Overall, as expected, LAIs were significantly more commonly used among patients with SMIs. Use of LAI antipsychotic in a small proportion of patients prior to assessment in the common mental disorder group could be possibly due to discrepancy in the diagnosis made at our centre and at the previous consultation. Previous studies which have evaluated the prescription patterns also suggest preference for oral medications in high proportion of cases, with use of LAIs in very small proportion of cases (Alosaimi et al., 2016; Grover et al., 2014, 2012; Levine et al., 2000; Xiang et al., 2012a, b). Although we did not evaluate, how much patients' decision was involved in the use of various formulations, but, still it can be said that exclusive use of oral preparations in the patients in their previous psychiatric treatment, possibly reflect the negative attitude of treating clinicians towards use of LAI antipsychotics, especially for patients with SMIs. Previous studies which have evaluated the attitude of mental health professionals towards LAI antipsychotics have also reported similar findings (Iyer et al., 2013a; Jaeger and Rossler, 2010; James et al., 2012; Patel et al., 2003). This suggests that there is a need to improve the awareness of mental health professionals about the beneficial effects of LAI antipsychotics, to improve the prescription rates of the same.

When the patients were asked regarding their preferred treatment, majority of patients irrespective of the diagnosis preferred tablets and other oral formulations over other treatments like LAIs and ECT. Although a small proportion of patients (12.7%) in the group-I (i.e., those with psychotic and bipolar disorder group) reported preference for injectables, the difference between those in group-I and group-II, was significant, suggesting that, higher proportion of patients with SMI prefer injectables and these must be offered to them. Additionally, in the present study, Injectables were chosen as first preferred choice in about 5.4%, as second preferred choice in about 9.1% and as third preferred choice by 7.3% of patients with SMI. If one compares the findings of the present study only, in terms of actual use of LAIs prior to recruitment into the study and preference to treatment, it is clearly evident that there is a gap in the rates of LAIs being prescribed by the mental health professionals and injectables being preferred by the patients. These findings further reiterate the fact that there is a need to make the clinicians aware of acceptability of injectables/LAIs by the patients and at least they should offer the same to all the patients with psychotic disorders, considered for long term antipsychotic medications. Present study also suggest lack of significant differences in preference for injectables between those with psychotic disorders and those with bipolar disorder, suggesting that injectables/LAIs are equally acceptable to patients with bipolar disorder and these must also be offered to this group of patients too. Higher rates of preference for injectables/LAIs, when compared to the actual practice may be reflective of the patient's own understanding of their illness, need for treatment, perceived benefits of injectables which are in general considered to be more potent and required for more severe ailments, experience of

Table 3
Comparison between Psychotic group and BPAD group.

Variables	Psychosis group (n = 321) Mean (SD)/ Frequency (%)	BPAD group (n = 120) Mean (SD)/ Frequency (%)	Chi-square/Mann-Whitney (p-value)
Duration of illness in months	50.38 (63.81)	34.09 (47.09)	U = 17329.0 (0.104)
Lifetime history of at least 1 episode of poor medication adherence in those who were on current treatment (n = 213)	157 (100%) (n = 157)	50 (89.3%) (n = 56)	**17.309 (< 0.001)***** **F = < 0.001*****
Past Psychiatric treatment			
Psychotherapy/counselling only	0 (0.0%)	2 (1.7%)	F = 0.074
Medication + Counselling	4 (1.2%)	1 (0.8%)	0.133 (0.716)Y
Tablets only	140(43.6%)	51 (42.5%)	0.29 (0.59)
Capsules only	1 (0.3%)	0 (0.0%)	F = 1.000
Injectables/LAI only	11 (3.4%)	2 (1.7%)	0.946 (0.331)
Combination of LAI and tablets	1 (0.3%)	0 (0.0%)	F = 1.000
No current treatment	164 (51.1%)	64 (53.3%)	**0.176 (0.674)**
Preferred treatment (Multiple answers)			
Psychotherapy/counselling only	**41(12.8%)**	**12 (10.0%)**	0.635(0.426)
Medication + Counselling	15 (4.7%)	6 (5.0%)	0.021 (0.886)
Tablets only	**149 (46.4%)**	**51 (42.5%)**	0.541 (0.462)
Capsules only	**40 (12.5%)**	**14 (11.7%)**	0.051(0.821)
Injectables/LAI only	**42 (13.1%)**	**14 (11.7%)**	0.158 (0.691)
ECT	8 (2.5%)	2 (1.7%)	0.269 (0.604)
Combination of tablets and capsules	10 (3.1%)	3 (2.5%)	0.116 (0.734)
Combination of LAI and tablets/capsules	**6 (1.9%)**	2 (1.7%)	0.020(0.887)
Medication and ECT	4 (1.2%)	1 (0.8%)	0.133 (0.716)Y
No specific preference	14 (4.4%)	2(1.7%)	1.814 (0.178)
Type of preferred treatment -First preference			
Psychotherapy/counselling only	35 (10.9%)	7 (5.8%)	2.60 (0.106)
Medication + Counselling	4 (1.2%)	2 (1.7%)	0.11 (0.73)Y
Tablets only	245 (76.3%)	100 (83.3%)	2.51 (0.112)
Capsules only	3 (0.9%)	0 (0%)	-
Injectables/LAI only	**16 (5.0%)**	**8 (6.7%)**	0.48 (0.488)
ECT	1 (0.3%)	0 (0%)	-
No preference – Left to doctor to decide	17 (5.3%)	3 (2.5%)	1.57 (0.209)
Second preference			
Psychotherapy/counselling only	1 (0.311%)	0 (0%)	-
Tablets only	11 (3.4%)	2 (1.7%)	0.945 (0.33)
Capsules only	25 (7.8%)	15 (12.5%)	2.35 (0.125)
Injectables/LAI only	**35 (10.9%)**	**8 (6.7%)**	1.78 (0.181)
No second preference – left to doctor to decide	249 (77.6%)	95 (79.2%)	0.12 (0.718)
Third preference			
Tablets only	1(0.3%)	0 (0.0%)	-
Capsules only	1 (0.3%)	0 (0.0%)	-
Injectables/LAI only	**21 (6.5%)**	**11 (9.2%)**	0.89 (0.344)
Combination of tablets and capsules	1 (0.3%)	0 (0.0%)	-
No third preference – left to doctor to decide	297 (92.5%)	109 (90.8%)	0.34 (0.558)
Will you prefer to take injectables?			
Yes	77 (24.0%)	26 (21.7%)	
No	225 (70.1%)	90 (75.0%)	1.616 (0.446)
Did not reply	19 (5.9%)	4 (3.3%)	
Have you ever taken been on any injectables? - Yes	71 (22.1%)	27 (22.5%)	0.007 (0.932)
Reasons for preference - if yes	(N = 77)	(N = 26)	
No problem in taking it	3 (3.89%)	0 (0.0%)	-
Problem with medicine	9 (11.68%)	2 (7.69%)	0.04 (0.83)Y
Easy	1 (1.29%)	2 (7.69%)	1.003 (0.316)Y
Long acting – have to take once in few days	1 (1.29%)	1 (3.84%)	0.0001 (0.99)Y
No specific reason	63(81.81%)	21(80.76%)	0.014 (0.905)
Reason for not preferring injectables	(n = 225)	(n = 90)	
No need	24 (10.66%)	7 (7.77%)	0.60 (0.436)
Difficulty to go to hospital to take injections	89 (39.55%)	30 (33.33%)	1.058 (0.303)
Uncomfortable with injection	1 (0.44%)	3 (3.33%)	2.28 (0.130)Y
Pain	51 (22.66%)	15 (16.66%)	0.533(0.464)
Prefer other type of medicines	20 (8.88%)	10 (11.11%)	0.368 (0.543)
Fear of injection	28 (12.44%)	19 (21.11%)	3.803 (0.051)
No specific reason	12 (5.33%)	6 (6.66%)	0.212 (0.645)

Y-Chi Square value with Yate's correction.

relapses with poor medication adherence,and understanding of their own detrimental behaviour towards own treatment. However, these variables were not evaluated as part of the present study. Overall, low rates of preference for injectables/LAIs in the present study could also be due to the fact that majority of patients and their caregivers are not aware of various treatment options including LAIs.

Majority of those patients, who opted for LAIs as a treatment option, were not able to give any specific reason (83.23%) for same. A small proportion of the patients reported reasons like problem with taking medicine (7.7%), convenience with LAIs, i.e., they have to take once in

few days (5.43%), no problem in taking injectables (1.96%) and an easy treatment option (1.35%). These findings again emphasize that LAIs are acceptable by a proportion of patients and the clinicians should consider the same. Therefore, patient-centred approach with shared decision making is needed in which patients are given all the available treatment options.We are not sure, why majority of the patients responded as no specific reason, but it is quite possible that the in depth interviews were not conducted to evaluate the same further. It would be interesting in future to evaluate this aspect further.

A significant finding of the present study includes significantly lower preference for LAIs among those who had received treatment in the past and had history of non-adherence. This result suggests that the preference for LAIs is significantly lower among those, who may actually benefit the most with the same. This could be due to poor knowledge about the LAIs or could be due to general reasons (fear of injectables, injectables being painful) for refusing any kind of injectables.

When the reasons for non-preferring LAIs were asked, the most common reason of the whole sample was difficulty in visiting the hospital frequently for administration of LAIs (41.69%) followed by pain (19.41%), fear of injections (13.96%) and considering it as no need (12.45%) and preferring other type of medications (8.52%).Significant difference was noted only for having no specific reason for refusal in patients with SMI (5.71%) as compared to patients with neurotic group of disorders (1.49%). Lack of insight and illness severity leading to poor understanding of the treatment options at the time of assessment could have possibly influenced this finding. Previous studies have reported embarrassment or shame associated with receiving LAIs/depot, feeling of being forced/coerced to take a LAI/depot, feelings of loss of control and concern over side-effects as major reasons for refusing LAIs (Iyer et al., 2013b; Patel et al., 2009, 2008; Sugawara et al., 2019). However, all these studies have evaluated patients who were enrolled or were mostly attending the depot clinics as a part of community assertive outreach programs in the Western countries, which could have influenced these responses too. Our findings are quite different from these findings and suggest that cultural factors and feasibility issues could have influenced such a decision. However, if one closely examines these responses it is evident that feasibility issues are the main reasons behind non-preference of LAIs. Possibly, in future with the availability of LAIs, which can be administered once in 3 to 6 months (such as Paliperidone Palmitate 3–monthly and 6 –monthly LAI)("A Study of Paliperidone Palmitate 6-Month Formulation - Tabular View - ClinicalTrials.gov," n.d.; Taylor and Huang, 2017), with reasonable cost can possibly improve these problems. Injection site pain and injection phobia are well-documented reasons for non-preference for any type of injectables across the age groups (McMurtry et al., 2015) and this holds good for LAIs too. Further, improving the technology for administration of LAIs by using painless techniques could improve the acceptability (Helfer, 2000; "Method and Device for Painless Injections - Available technology for licensing from the University of California, Irvine," n.d.).

In the present study, lifetime history of at least one episode (not taking the prescribed medications continuously for few days) of poor medication adherence pertaining to psychotropics in those patients who had a previous history of receiving psychiatric treatment was 90%. This figure is in the reported range for medication non-adherence in the literature [up to 89% in schizophrenia (Lacro et al., 2002; Velligan et al., 2009), 60–70% in bipolar disorder (Montes et al., 2013), about 52% in depression (Julius et al., 2009) and approximately 50% in patients with anxiety disorders (Santana and Fontenelle, 2011; Toni et al., 2004)]. Medication non-adherence rates were significantly higher in the psychotic and bipolar group when compared to those diagnosed with neurotic, stress related and depressive disorder group. This has been well-researched across several studies. Studies which have compared the medication non-adherence across these broad groups have been inconclusive, with some of the studies reporting higher rate of medication non-adherence among those with SMIs when compared to common mental disorders (Clatworthy et al., 2007; Julius et al., 2009; Semahegn et al., 2018; Stein-Shvachman et al., 2013), whereas others suggest the reverse (Cramer and Rosenheck, 1998; DiMatteo et al., 2000). Findings of the present study support the prior group of studies. Present study suggests significant difference in the rate of medication non-adherence between patients with psychotic disorders and those with bipolar disorder who had received psychiatric treatment in the past with significantly higher rates of non-adherence in patients with psychotic disorders than bipolar disorder. This finding is in commensurate with the existing literature which is almost equivocal about prevalence rates of non-adherence among patients with schizophrenia and bipolar disorder (García et al., 2016; Semahegn et al., 2018).

Limitations of the study LAI antipsychotics include use of a brief self-designed questionnaire to assess the acceptability of the various treatments, especially LAIs. Present study did not involve in depth interviews and reasons for non-adherence. Illness related factors like disorder specific characteristics, severity and insight could have influenced the responses. However, such an association was not evaluated. Further, the choice of the treatment could also be influenced by the diagnostic categories, such as neurotic patients, would prefer to take milder treatments, such as tablets and psychotherapy. We specifically did not evaluate this fact.

In the era of psychiatric advance directives and patient-centred medicine, providing information about medication preferences may increase prescribing of patient-preferred medications (Wilder et al., 2010) and can be more useful in improving adherence to treatment outcomes (Eiring et al., 2015). Considering the fact that LAIs are highly underused in patients with SMI and there is lack of awareness about LAIs among patients with SMI as well as psychiatrists' own inhibitions to use the same, the present study findings suggest that there is reasonable level of acceptance of LAIs (21–24%) among patients with SMI and a substantial proportion of patients (5–10%) with SMI would prefer to take LAI, highlights the fact that LAIs could be a preferred treatment option of the patients which should be taken into consideration while making treatment decisions.

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Declaration of Competing Interest

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References

Ahn, J., McCombs, J.S., Jung, C., Croudace, T.J., McDonnell, D., Ascher-Svanum, H., Edgell, E.T., Shi, L., 2008. Classifying patients by antipsychotic adherence patterns using latent class analysis: characteristics of nonadherent groups in the California Medicaid (Medi-Cal) program. Value Health J. Int. Soc. Pharmacoecon. Outcomes Res. 11, 48–56. https://doi.org/10.1111/j.1524-4733.2007.00214.x.

Alosaimi, F.D., Alhabbad, A., Abalhassan, M.F., Fallata, E.O., Alzain, N.M., Alassiry, M.Z., Haddad, B.A., 2016. Patterns of psychotropic medication use in inpatient and outpatient psychiatric settings in Saudi Arabia. Neuropsychiatr. Dis. Treat. 12, 897–907. https://doi.org/10.2147/NDT.S100405.

Brissos, S., Veguilla, M.R., Taylor, D., Balanzá-Martinez, V., 2014. The role of long-acting injectable antipsychotics in schizophrenia: a critical appraisal. Ther. Adv. Psychopharmacol. 4, 198–219. https://doi.org/10.1177/2045125314540297.

Caroli, F., Raymondet, P., Izard, I., Plas, J., Gall, B., Delgado, A., 2011. Opinions of French patients with schizophrenia regarding injectable medication. Patient Prefer. Adherence 5, 165–171. https://doi.org/10.2147/PPA.S15337.

Chapman, S.C.E., Horne, R., 2013. Medication nonadherence and psychiatry. Curr. Opin. Psychiatry 26, 446–452. https://doi.org/10.1097/YCO.0b013e3283642da4.

Clatworthy, J., Bowskill, R., Rank, T., Parham, R., Horne, R., 2007. Adherence to medication in bipolar disorder: a qualitative study exploring the role of patients' beliefs about the condition and its treatment. Bipolar Disord. 9, 656–664. https://doi.org/10.1111/j.1399-5618.2007.00434.x.

Coldham, E.L., Addington, J., Addington, D., 2002. Medication adherence of individuals

with a first episode of psychosis. Acta Psychiatr. Scand. 106, 286–290.
Cramer, J.A., Rosenheck, R., 1998. Compliance with medication regimens for mental and physical disorders. Psychiatr. Serv. 49, 196–201. https://doi.org/10.1176/ps.49.2.196.
DiMatteo, M.R., Lepper, H.S., Croghan, T.W., 2000. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. Arch. Intern. Med. 160, 2101–2107. https://doi.org/10.1001/archinte.160.14.2101.
Dufort, A., Zipursky, R.B., 2019. Understanding and managing treatment adherence in schizophrenia. Clin. Schizophr. Relat. Psychoses. https://doi.org/10.3371/CSRP.ADRZ.121218.
Eiring, Ø., Landmark, B.F., Aas, E., Salkeld, G., Nylenna, M., Nytrøen, K., 2015. What matters to patients? A systematic review of preferences for medication-associated outcomes in mental disorders. BMJ Open 5, e007848. https://doi.org/10.1136/bmjopen-2015-007848.
El-Khayat, R., Baldwin, D.S., 1998. Antipsychotic drugs for non-psychotic patients: assessment of the benefit/risk ratio in generalized anxiety disorder. J. Psychopharmacol. (Oxf.) 12, 323–329. https://doi.org/10.1177/026988119801200401.
Fayek, M., Flowers, C., Signorelli, D., Simpson, G., 2003. Psychopharmacology: underuse of evidence-based treatments in psychiatry. Psychiatr. Serv. Wash. DC 54 (1453–1454), 1456. https://doi.org/10.1176/appi.ps.54.11.1453.
Fleischhacker, W.W., Eerdekens, M., Karcher, K., Remington, G., Llorca, P.-M., Chrzanowski, W., Martin, S., Gefvert, O., 2003. Treatment of schizophrenia with long-acting injectable risperidone: a 12-month open-label trial of the first long-acting second-generation antipsychotic. J. Clin. Psychiatry 64, 1250–1257.
García, S., Martínez-Cengotitabengoa, M., López-Zurbano, S., Zorrilla, I., López, P., Vieta, E., González-Pinto, A., 2016. Adherence to antipsychotic medication in bipolar disorder and schizophrenic patients. J. Clin. Psychopharmacol. 36, 355–371. https://doi.org/10.1097/JCP.0000000000000523.
Giraud-Baro, E., Dassa, D., De Vathaire, F., Garay, R.P., Obeid, J., 2016. Schizophrenia-spectrum patients treated with long-acting injectable risperidone in real-life clinical settings: functional recovery in remitted versus stable, non-remitted patients (the EVeREST prospective observational cohort study). BMC Psychiatry 16, 8. https://doi.org/10.1186/s12888-016-0712-1.
Goodnick, P.J., Barrios, C.A., 2001. Use of olanzapine in non-psychotic psychiatric disorders. Expert Opin. Pharmacother. 2, 667–680. https://doi.org/10.1517/14656566.2.4.667.
Grover, S., Kumar, V., Avasthi, A., Kulhara, P., 2012. An audit of first prescription of new patients attending a psychiatry walk-in-clinic in north India. Indian J. Pharmacol. 44, 319–325. https://doi.org/10.4103/0253-7613.96302.
Grover, S., Avasthi, A., Sinha, V., Lakdawala, B., Bathla, M., Sethi, S., Mathur, D.M., Kathuria, P., Shah, S., Baalasubramanian, D.S., Agarwal, V., Deka, K., 2014. Indian Psychiatric Society multicentric study: prescription patterns of psychotropics in India. Indian J. Psychiatry 56, 253–264. https://doi.org/10.4103/0019-5545.140632.
Haddad, P.M., Brain, C., Scott, J., 2014. Nonadherence with antipsychotic medication in schizophrenia: challenges and management strategies. Patient Relat. Outcome Meas. 5, 43–62. https://doi.org/10.2147/PROM.S42735.
Helfer, J., 2000. Painless injections: heifer skin tap technique. Nurse Educ. 25, 272–273.
Heres, S., Hamann, J., Kissling, W., Leucht, S., 2006. Attitudes of psychiatrists toward antipsychotic depot medication. J. Clin. Psychiatry 67, 1948–1953.
Heres, S., Schmitz, F.S., Leucht, S., Pajonk, F.-G., 2007. The attitude of patients towards antipsychotic depot treatment. Int. Clin. Psychopharmacol. 22, 275–282. https://doi.org/10.1097/YIC.0b013e3280c28424.
Hoencamp, E., Knegtering, H., Kooy, U.S., Van Der Molen, A.E.G.M., 1995. Patient requests and attitude towards neuroleptics. Nord. J. Psychiatry 49, 47–55. https://doi.org/10.3109/08039489509099720.
Hugtenburg, J.G., Timmers, L., Elders, P.J., Vervloet, M., van Dijk, L., 2013. Definitions, variants, and causes of nonadherence with medication: a challenge for tailored interventions. Patient Prefer. Adherence 7, 675–682. https://doi.org/10.2147/PPA.S29549.
Iyer, S., Banks, N., Roy, M.-A., Tibbo, P., Williams, R., Manchanda, R., Chue, P., Malla, A., 2013a. A qualitative study of experiences with and perceptions regarding long-acting injectable antipsychotics: part II-physician perspectives. Can. J. Psychiatry Rev. Can. Psychiatr. 58, 23S–29S.
Iyer, S., Banks, N., Roy, M.-A., Tibbo, P., Williams, R., Manchanda, R., Chue, P., Malla, A., 2013b. A qualitative study of experiences with and perceptions regarding long-acting injectable antipsychotics: Part I-patient perspectives. Can. J. Psychiatry Rev. Can. Psychiatr. 58, 14S–22S.
Jaeger, M., Rossler, W., 2010. Attitudes towards long-acting depot antipsychotics: a survey of patients, relatives and psychiatrists. Psychiatry Res. 175, 58–62. https://doi.org/10.1016/j.psychres.2008.11.003.
James, B.O., Omoaregba, J.O., Okonoda, K.M., Otefe, E.U., Patel, M.X., 2012. The knowledge and attitudes of psychiatrists towards antipsychotic long-acting injections in Nigeria. Ther. Adv. Psychopharmacol. 2, 169–177. https://doi.org/10.1177/2045125312453158.
Julius, R.J., Novitsky, M.A., Dubin, W.R., 2009. Medication adherence: a review of the literature and implications for clinical practice. J. Psychiatr. Pract. 15, 34–44. https://doi.org/10.1097/01.pra.0000344917.43780.77.
Kim, B., Lee, S.-H., Yang, Y.K., Park, J.-I., Chung, Y.-C., 2012. Long-acting injectable antipsychotics for first-episode schizophrenia: the pros and cons. Schizophr. Res. Treat. 2012. https://doi.org/10.1155/2012/560836.
Lacro, J.P., Dunn, L.B., Dolder, C.R., Leckband, S.G., Jeste, D.V., 2002. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. J. Clin. Psychiatry 63, 892–909.
Larsen, E.B., Gerlach, J., 1996. Subjective experience of treatment, side-effects, mental state and quality of life in chronic schizophrenic out-patients treated with depot neuroleptics. Acta Psychiatr. Scand. 93, 381–388. https://doi.org/10.1111/j.1600-0447.1996.tb10664.x.
Leucht, C., Heres, S., Kane, J.M., Kissling, W., Davis, J.M., Leucht, S., 2011. Oral versus depot antipsychotic drugs for schizophrenia—A critical systematic review and meta-analysis of randomised long-term trials. Schizophr. Res. 127, 83–92. https://doi.org/10.1016/j.schres.2010.11.020.
Levine, J., Chengappa, K.N., Brar, J.S., Gershon, S., Yablonsky, E., Stapf, D., Kupfer, D.J., 2000. Psychotropic drug prescription patterns among patients with bipolar I disorder. Bipolar Disord. 2, 120–130.
Lingam, R., Scott, J., 2002. Treatment non-adherence in affective disorders. Acta Psychiatr. Scand. 105, 164–172.
Llorca, P.-M., Sacchetti, E., Lloyd, K., Kissling, W., Medori, R., 2008. Long-term remission in schizophrenia and related psychoses with long-acting risperidone: results obtained in an open-label study with an observation period of 18 months. Int. J. Clin. Pharmacol. Ther. 46, 14–22. https://doi.org/10.5414/cpp46014.
Llorca, P.M., Abbar, M., Courtet, P., Guillaume, S., Lancrenon, S., Samalin, L., 2013. Guidelines for the use and management of long-acting injectable antipsychotics in serious mental illness. BMC Psychiatry 13, 340. https://doi.org/10.1186/1471-244X-13-340.
Malla, A.K., Norman, R.M.G., Manchanda, R., Townsend, L., 2002. Symptoms, cognition, treatment adherence and functional outcome in first-episode psychosis. Psychol. Med. 32, 1109–1119. https://doi.org/10.1017/S0033291702006050.
Malla, A., Tibbo, P., Chue, P., Levy, E., Manchanda, R., Teehan, M., Williams, R., Iyer, S., Roy, M.-A., 2013. Long-acting injectable antipsychotics: recommendations for clinicians. Can. J. Psychiatry Rev. Can. Psychiatr. 58, 30S–35S.
Manchanda, R., Chue, P., Malla, A., Tibbo, P., Roy, M.-A., Williams, R., Iyer, S., Lutgens, D., Banks, N., 2013. Long-acting injectable antipsychotics: evidence of effectiveness and use. Can. J. Psychiatry Rev. Can. Psychiatr. 58, 5S–13S.
Marcum, Z.A., Sevick, M.A., Handler, S.M., 2013. Medication non adherence. JAMA J. Am. Med. Assoc. 309, 2105–2106. https://doi.org/10.1001/jama.2013.4638.
McMurtry, C.M., Noel, M., Taddio, A., Antony, M.M., Asmundson, G.J.G., Riddell, R.P., Chambers, C.T., Shah, V., 2015. Interventions for individuals with high levels of needle fear. Clin. J. Pain 31, S109–S123. https://doi.org/10.1097/AJP.0000000000000273.
Miyamoto, S., Wolfgang Fleischhacker, W., 2017. The use of long-acting injectable antipsychotics in schizophrenia. Curr. Treat. Options Psychiatry 4, 117–126. https://doi.org/10.1007/s40501-017-0115-z.
Montes, J.M., Maurino, J., de Dios, C., Medina, E., 2013. Suboptimal treatment adherence in bipolar disorder: impact on clinical outcomes and functioning. Patient Prefer. Adherence 7, 89–94. https://doi.org/10.2147/PPA.S39290.
Nasrallah, H.A., Duchesne, I., Mehnert, A., Janagap, C., Eerdekens, M., 2004. Health-related quality of life in patients with schizophrenia during treatment with long-acting, injectable risperidone. J. Clin. Psychiatry 65, 531–536.
Nosé, M., Barbui, C., Gray, R., Tansella, M., 2003. Clinical interventions for treatment non-adherence in psychosis: meta-analysis. Br. J. Psychiatry J. Ment. Sci. 183, 197–206.
Patel, M.X., Nikolaou, V., David, A.S., 2003. Psychiatrists' attitudes to maintenance medication for patients with schizophrenia. Psychol. Med. 33, 83–89.
Patel, M.X., de Zoysa, N., Bernadt, M., David, A.S., 2008. A cross-sectional study of patients' perspectives on adherence to antipsychotic medication: depot versus oral. J. Clin. Psychiatry 69, 1548–1556.
Patel, M.X., De Zoysa, N., Bernadt, M., David, A., 2009. Depot and oral antipsychotics: patient preferences and attitudes are not the same thing. J. Psychopharmacol. Oxf. Engl. 23, 789–796. https://doi.org/10.1177/0269881108092124.
Pereira, S., Pinto, R., 1997. A survey of the attitudes of chronic psychiatric patients living in the community toward their medication. Acta Psychiatr. Scand. 95, 464–468.
Samalin, L., Charpeaud, T., Blanc, O., Heres, S., Llorca, P.-M., 2013. Clinicians' attitudes toward the use of long-acting injectable antipsychotics. J. Nerv. Ment. Dis. 201, 553–559. https://doi.org/10.1097/NMD.0b013e31829829c4.
Santana, L., Fontenelle, L.F., 2011. A review of studies concerning treatment adherence of patients with anxiety disorders. Patient Prefer. Adherence 5, 427–439. https://doi.org/10.2147/PPA.S23439.
Semahegn, A., Torpey, K., Manu, A., Assefa, N., Tesfaye, G., Ankomah, A., 2018. Psychotropic medication non-adherence and associated factors among adult patients with major psychiatric disorders: a protocol for a systematic review. Syst. Rev. 7. https://doi.org/10.1186/s13643-018-0676-y.
Stein-Shvachman, I., Karpas, D.S., Werner, P., 2013. Depression treatment non-adherence and its psychosocial predictors: differences between young and older adults? Aging Dis. 4, 329–336. https://doi.org/10.14336/AD.2013.0400329.
Stevens, G.L., Dawson, G., Zummo, J., 2016. Clinical benefits and impact of early use of long-acting injectable antipsychotics for schizophrenia. Early Interv. Psychiatry 10, 365–377. https://doi.org/10.1111/eip.12278.
Sugawara, N., Kudo, S., Ishioka, M., Sato, Y., Kubo, K., Yasui-Furukori, N., 2019. Attitudes toward long-acting injectable antipsychotics among patients with schizophrenia in Japan. Neuropsychiatr. Dis. Treat. 15, 205–211. https://doi.org/10.2147/NDT.S188337.
Taylor, M., Huang, H.C.-H., 2017. A stitch in time: 3-monthly long-acting injectable paliperidone palmitate in schizophrenia. Ther. Adv. Psychopharmacol. 7, 231–233. https://doi.org/10.1177/2045125317721874.
Toni, C., Perugi, G., Frare, F., Mata, B., Akiskal, H.S., 2004. Spontaneous treatment discontinuation in panic disorder patients treated with antidepressants. Acta Psychiatr. Scand. 110, 130–137. https://doi.org/10.1111/j.1600-0047.2004.00347.x.
Veale, D., Miles, S., Smallcombe, N., Ghezai, H., Goldacre, B., Hodsoll, J., 2014. Atypical antipsychotic augmentation in SSRI treatment refractory obsessive-compulsive disorder: a systematic review and meta-analysis. BMC Psychiatry 14, 317. https://doi.

org/10.1186/s12888-014-0317-5.
Velligan, D.I., Weiden, P.J., Sajatovic, M., Scott, J., Carpenter, D., Ross, R., Docherty, J.P., Expert Consensus Panel on Adherence Problems in Serious and Persistent Mental Illness, 2009. The expert consensus guideline series: adherence problems in patients with serious and persistent mental illness. J. Clin. Psychiatry 70 (Suppl. 4), 1–46 quiz 47–48.
Velligan, D.I., Weiden, P.J., Sajatovic, M., Scott, J., Carpenter, D., Ross, R., Docherty, J.P., 2010a. Assessment of adherence problems in patients with serious and persistent mental illness: recommendations from the Expert Consensus Guidelines. J. Psychiatr. Pract. 16, 34–45. https://doi.org/10.1097/01.pra.0000367776.96012.ca.
Velligan, D.I., Weiden, P.J., Sajatovic, M., Scott, J., Carpenter, D., Ross, R., Docherty, J.P., 2010b. Strategies for addressing adherence problems in patients with serious and persistent mental illness: recommendations from the expert consensus guidelines. J. Psychiatr. Pract. 16, 306–324. https://doi.org/10.1097/01.pra.0000388626.98662.a0.
Waddell, L., Taylor, M., 2009. Attitudes of patients and mental health staff to antipsychotic long-acting injections: systematic review. Br. J. Psychiatry Suppl. 52, S43–50. https://doi.org/10.1192/bjp.195.52.s43.
Walburn, J., Gray, R., Gournay, K., Quraishi, S., David, A.S., 2001. Systematic review of patient and nurse attitudes to depot antipsychotic medication. Br. J. Psychiatry J. Ment. Sci. 179, 300–307.
Warren, B., 1998. Developing practice through clinical audit. J. Clin. Eff. 3, 151–155. https://doi.org/10.1108/eb020891.
Wilder, C.M., Elbogen, E.B., Moser, L.L., Swanson, J.W., Swartz, M.S., 2010. Medication preferences and adherence among individuals with severe mental illness and psychiatric advance directives. Psychiatr. Serv. Wash. DC 61, 380–385. https://doi.org/10.1176/ps.2010.61.4.380.
Xiang, Yu-Tao, Hu, C., Wang, G., Zheng, Q.-W., Fang, Y.-R., Ungvari, G.S., Kilbourne, A.M., Lai, K.Y.C., Si, T.-M., Chen, D.-F., Lu, Z., Yang, H.-C., Hu, J., Chen, Z.-Y., Huang, Y., Sun, J., Wang, X.-P., Li, H.-C., Zhang, J.-B., Chiu, H.F.K., 2012a. Prescribing patterns of antidepressants, antipsychotics and mood stabilizers in bipolar patients misdiagnosed with major depressive disorder in China. Hum. Psychopharmacol. 27, 626–631. https://doi.org/10.1002/hup.2262.
Xiang, Y.-T., Wang, C.-Y., Si, T.-M., Lee, E.H.M., He, Y.-L., Ungvari, G.S., Chiu, H.F.K., Yang, S.-Y., Chong, M.-Y., Tan, C.-H., Kua, E.-H., Fujii, S., Sim, K., Yong, K.H., Trivedi, J.K., Chung, E.-K., Udomratn, P., Chee, K.-Y., Sartorius, N., Shinfuku, N., 2012b. Antipsychotic polypharmacy in inpatients with schizophrenia in Asia (2001–2009). Pharmacopsychiatry 45, 7–12. https://doi.org/10.1055/s-0031-1286345.
Yatham, L.N., Goldstein, J.M., Vieta, E., Bowden, C.L., Grunze, H., Post, R.M., Suppes, T., Calabrese, J.R., 2005. Atypical antipsychotics in bipolar depression: potential mechanisms of action. J. Clin. Psychiatry 66 (Suppl. 5), 40–48.