SMER
Society of Medical Education & Research

2021, Volume 1, Page No: 152-167
ISSN: 3108-4826

Society of Medical Education & Research

Journal of Medical Sciences and Interdisciplinary Research

Perspectives and Experiences of Patients, Caregivers, and Healthcare Providers Regarding Long-Acting Injectable Antipsychotics in Schizophrenia Treatment: Qualitative Findings from the Multinational ADVANCE Study

Katarina Milena Petrovic[1]*, Jelena Ivana Markovic[1]

[1]Department of Management, Faculty of Economics, University of Novi Sad, Novi Sad, Serbia.

***E-mail** ✉ k.petrovic.novisad@gmail.com

Abstract

Schizophrenia represents a chronic and debilitating mental disorder that significantly affects patients' daily functioning and creates societal challenges. Long-acting injectable antipsychotics (LAIs) have been shown to enhance adherence and lower relapse and hospitalization rates compared with oral antipsychotic treatments, yet their adoption differs widely between countries. The qualitative portion of the global ADVANCE study (Attitudes DriVing regional differences in long-acting injectable ANtipsychotic utilization for schizophrenia among healthcare professionals, patients, and CaregivErs) sought to explore how patients experience the journey from diagnosis to treatment, their goals, and their perspectives on LAIs, as well as how these factors may influence acceptance and use. The study included psychiatrists, psychiatric nurses, adults living with schizophrenia, and caregivers from eight countries: Australia, Canada, China, Germany, Israel, Spain, South Korea, and the United States. Eligible HCPs devoted the majority of their workweek (≥65%) to direct patient care, managed adult populations in which at least 10% were diagnosed with schizophrenia, and had prescribed second-generation LAIs within the past year. Patients were adults (≥18 years) with schizophrenia, and caregivers were included if they had experience with LAI treatment for the patient in their care. Data were collected via 60-minute semi-structured telephone interviews. Interviews were completed by 17 HCPs, 20 patients, and 19 caregivers. HCPs described a recurring cycle in which patients often experienced relapse following treatment, with inpatient services focused on immediate symptom management and outpatient care emphasizing sustained quality of life. Major barriers to LAI adoption reported by HCPs included injection reluctance, logistical hurdles, and previous traumatic experiences related to compulsory injections. Patients' experiences highlighted two primary care trajectories: (1) early-stage intervention with strong outpatient support, and (2) severe acute episodes necessitating hospitalization. Those whose initial care was outpatient were generally more receptive to LAIs, whereas individuals who first experienced inpatient treatment frequently reported fear, feelings of disempowerment, and hesitancy toward LAIs for long-term management. Caregivers were primarily concerned with maintaining patients' quality of life and were actively involved in disease management. The nature of interactions between patients and psychiatric professionals varies depending on whether care is delivered in inpatient or outpatient settings, influencing LAI acceptance. Factors such as initial symptom presentation, family involvement, hospitalization history, trust in HCPs, and logistical constraints all appear to shape patients' attitudes toward LAIs and overall outcomes.

Keywords: Schizophrenia, Long-acting injectable antipsychotics, Patients, caregivers, Healthcare professionals, Setting of care, Treatment preference

Access this article online https://smerpub.com/

Received: 27 May 2021; **Accepted:** 05 September 2021

How to cite this article: Petrovic KM, Markovic JI. Perspectives and Experiences of Patients, Caregivers, and Healthcare Providers Regarding Long-Acting Injectable Antipsychotics in Schizophrenia Treatment: Qualitative Findings from the Multinational ADVANCE Study. J Med Sci Interdiscip Res. 2021;1:152-67. https://doi.org/10.51847/R39whqtn7i

Introduction

Schizophrenia is a lifelong, progressive mental disorder that can lead to significant functional decline and disability [1, 2]. Worldwide, about 24 million individuals live with schizophrenia, and prevalence is rising [3, 4].

Patients commonly experience hallucinations, delusions, and cognitive disturbances that interfere with day-to-day functioning [5], with repeated relapses increasing risks of self-harm and limiting educational or occupational achievements [6]. The disorder heavily affects both patients' and their families' quality of life [2], with caregivers often assuming substantial responsibilities ranging from daily living assistance to emotional and financial support [7, 8].

Traditionally, oral antipsychotics have been the cornerstone of treatment, yet adherence is frequently suboptimal [9, 10]. In recent years, the availability of LAIs has expanded, offering longer-lasting treatment options [11, 12]. These medications improve adherence, which contributes to reduced relapse rates and fewer hospitalizations compared with oral therapy [13]. The ability to administer LAIs in multiple care settings facilitates monitoring, enabling early identification of missed doses or discontinuation.

Evidence increasingly supports using LAIs early in the disease course, including for first-episode psychosis, though many clinicians still reserve them for patients with poor adherence or severe symptoms [13–15]. Higher LAI prescription rates are observed among younger HCPs, those with larger caseloads of schizophrenia patients, and professionals practicing in academic or community settings [10, 16]. Patients more often prescribed LAIs include men, those with lower education levels, or individuals lacking family support [17–19]. In certain countries, such as France and the US, patients with caregiver support are more likely to receive LAIs [18, 19].

Despite clear clinical benefits, LAI use varies internationally, and the reasons for these differences remain unclear [9, 13, 19–21]. Large-scale, multinational research is needed to better understand the factors driving LAI uptake, which could inform strategies to enhance adoption and improve outcomes. Exploring patients' treatment pathways, goals, management experiences, and perceptions of LAIs is crucial [20, 21].

The ADVANCE study aimed to address this gap by investigating the attitudes of patients, caregivers, and HCPs toward LAIs in multiple countries [22, 23]. The study included two phases: qualitative interviews and a quantitative survey. This manuscript reports findings from the qualitative phase, which sought to understand (1) the patient journey from diagnosis through ongoing care, (2) treatment goals and HCP qualities that influence decisions, and (3) experiences and perceptions regarding LAIs, including recommendations, decision-making, and perceived benefits and limitations.

Materials and Methods

HCP participants: psychiatrists and psychiatric nurses

Eligible participants included psychiatrists and psychiatric nurses who spent the majority of their time providing direct care, managed adult populations with at least 10% diagnosed with schizophrenia, and had treated patients with second-generation LAIs within the last twelve months. Recruitment targeted eight countries: Australia, Canada, China, Germany, Israel, Spain, South Korea, and the US. The initial goal was to enroll one psychiatrist and one nurse per country; flexibility was allowed based on recruitment feasibility. Potential participants were identified through Capvision panels, professional networks such as LinkedIn, and publicly available medical publication databases. Outreach focused on individuals with relevant clinical experience within targeted therapeutic areas and geographic regions. Respondents who expressed interest completed a 20-minute online screening survey that collected information on clinical setting, patient caseload, and experience with LAIs. Qualification for participation was based solely on responses to this screening. In South Korea, psychiatric nurses could not be recruited due to local compliance restrictions, so only psychiatrists participated.

Patient and caregiver participants

Patients were eligible if they were at least 18 years old, had a schizophrenia diagnosis, were currently receiving antipsychotic treatment, and had either personal experience with LAIs or had been recommended an LAI by their physician. Caregivers were eligible if they were involved in the care and treatment of an individual with schizophrenia who met the same inclusion criteria for patients and had either received or been recommended LAI treatment. Importantly, caregivers in this study were not connected to the patient participants. Recruitment included individuals from Australia, Canada, China, Germany, Israel, Spain, South Korea, and the United States. A larger sample of patients and caregivers was recruited compared with HCPs to address the limited existing research on their perspectives.

In Australia, Canada, Germany, Israel, Spain, and the US, recruitment relied on digital outreach, social media campaigns, and online community groups. In China, recruitment was primarily through HCP recommendations within a vendor's panel. In South Korea, participants were identified either via HCP referrals or a local vendor database. Eligibility was confirmed through a 20-minute online screening interview for both patients and caregivers.

Interview procedures

Interviews were conducted via video or audio calls by trained researchers who had no prior relationship with participants. Each session lasted approximately 60 minutes. Interviews with HCPs were conducted between May and July 2023, while patient and caregiver interviews took place from June to November 2023.

A semi-structured interview guide, specifically developed for this study, was used across all participant groups. The guides were designed to explore factors potentially affecting LAI use at a country level, drawing from three sources: 1) literature review identifying barriers and facilitators of LAI adoption, 2) published evidence on patient and caregiver beliefs and experiences with LAIs, and 3) country-specific market assessments of LAI use and systemic influences. The guides were refined iteratively through team discussions and expert review.

Separate guides were tailored for HCPs, patients, and caregivers. HCP interviews explored professional background, patient population, treatment strategies for schizophrenia, and experiences with LAIs. Patient interviews examined their personal history with schizophrenia, current experiences, and perceptions of LAIs. Caregiver interviews focused on the individual they cared for, the patient's history of schizophrenia, and experiences with LAI treatment.

Data analysis

All interviews were audio-recorded and transcribed verbatim, with any personally identifiable information removed. Notes were taken during and after each interview to capture participants' responses, and recordings were referenced to address any gaps. Responses were systematically reviewed, categorized, and coded based on recurring themes, key concepts, and relevant terminology. No formal analytic framework was applied; the analysis focused on identifying and quantifying patterns within the qualitative data.

Results and Discussion

HCP participants: psychiatrists and psychiatric nurses

Participant characteristics

Of the 1,250 HCPs initially contacted, 31 completed screening, and 17 were ultimately invited for the full interview. Participants were selected from those who responded first and met inclusion criteria. The sample included 10 psychiatrists (7 male, 3 female) and 7 psychiatric nurses (2 male, 5 female) from Australia (n = 2), Canada (n = 2), China (n = 3), Germany (n = 2), Israel (n = 3), South Korea (n = 1), Spain (n = 2), and the US (n = 2). Psychiatrists had an average of 18 years of clinical experience (range: 4–40 years), while psychiatric nurses averaged 17 years (range: 4–32 years).

Most psychiatrists and psychiatric nurses primarily practiced in hospital-based outpatient clinics (45 percent and 20 percent, respectively), inpatient psychiatric wards (24 percent and 28 percent), community mental health or psychiatric outpatient centers (19 percent and 47 percent), or private/independent practices (12 percent and 5 percent) **(Table 1).**

Table 1. Characteristics of HCPs (N = 17)

Country	HCP Role	% of Patients on LAIs	Clinical Experience (years)	Main Practice Setting
Australia	Psychiatrist	40	10	Hospital-based outpatient clinic
	Psychiatric Nurse	5	32	Community/psychiatric outpatient clinic
Canada	Psychiatrist	40	27	Inpatient psychiatric ward
	Psychiatric Nurse	50	28	Inpatient psychiatric ward
China	Psychiatrist	10	40	Inpatient psychiatric ward
	Psychiatrist	10	34	Hospital-based outpatient / inpatient ward
	Psychiatric Nurse	5	6	Inpatient psychiatric ward
Germany	Psychiatrist	20	10	Hospital-based outpatient clinic
	Psychiatric Nurse	20	4	Hospital-based outpatient clinic
Israel	Psychiatrist	30	6	Community/psychiatric outpatient clinic
	Psychiatrist	10	6	Community/psychiatric outpatient clinic

	Psychiatric Nurse	30	10	Inpatient psychiatric ward
South Korea	Psychiatrist	30	10	Hospital-based outpatient clinic
Spain	Psychiatrist	30	4	Hospital-based outpatient clinic
	Psychiatric Nurse	40	25	Community/psychiatric outpatient clinic
United States	Psychiatrist	50	35	Community/psychiatric outpatient / inpatient ward
	Psychiatric Nurse	60	11	Community/psychiatric outpatient clinic

Treatment goals and clinical decision-making

According to HCPs, the primary treatment goals for patients with schizophrenia included controlling and stabilizing positive symptoms (65 percent), enhancing patient quality of life (47 percent), preventing physical harm to the patient or staff (24 percent), managing negative symptoms (24 percent), and minimizing side effects (12 percent) **(Figure 1)**. Emphasizing the dual focus on symptom control and life quality, one HCP remarked, "We are so focused on psychotic functions because we're afraid they'll do something really bad, but they want just to connect again with the world."

When responses were examined by HCP type, psychiatrists most frequently identified stabilizing and managing positive symptoms (90 percent), preventing physical harm (30 percent), and improving patient quality of life (30 percent) as key objectives. In contrast, psychiatric nurses prioritized improving patient quality of life (71 percent), followed by controlling positive symptoms (29 percent) and preventing harm (14 percent).

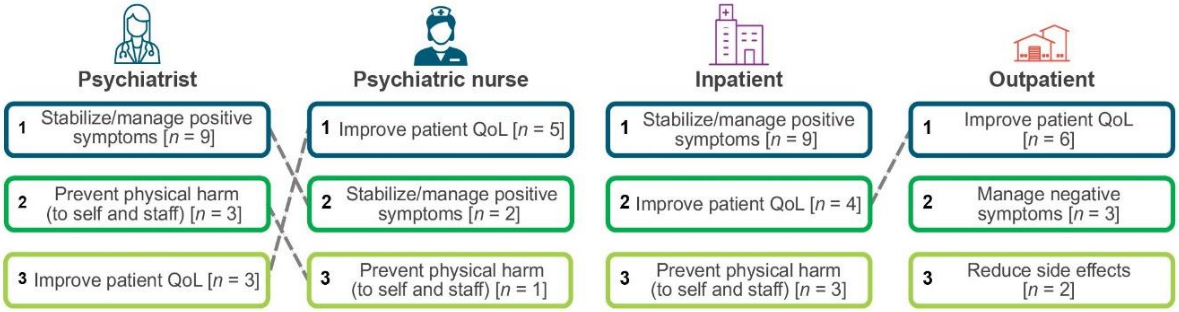


Figure 1. HCP-reported treatment goals. HCP= healthcare professional; QoL= quality of life.

HCP-reported treatment objectives differed depending on the care setting **(Figure 1)**. In inpatient settings, the three most frequently cited goals were controlling and stabilizing positive symptoms (53%), enhancing patient quality of life (24%), and preventing harm to patients or staff (18%). In outpatient settings, the primary objectives shifted to improving patient quality of life (35%), managing negative symptoms (18 percent), and reducing side effects (12%).

In Australia, Canada, and Germany, HCPs reported that public inpatient care is fully covered and paid for, which can influence patient care decisions. In these countries, some patients prefer inpatient care via the emergency department over outpatient services with community psychiatrists due to cost differences. Across Australia, Canada, China, Germany, and Israel, HCPs noted a shortage of community psychiatrists, leading to extended wait times for outpatient appointments.

Treatment discussions in inpatient settings were primarily led by psychiatrists, with a focus on stabilizing patients and managing positive symptoms. In outpatient care, general practitioners often led initial discussions, particularly in Australia, Canada, and Israel, though they frequently consulted psychiatrists if treatment adjustments were required. Psychiatric nurses generally reported having low to moderate influence in treatment decision-making across both care settings.

LAI use

Psychiatrists reported an average LAI usage of 27 percent, ranging from 10 percent in China and Israel to 50% in the United States. Psychiatric nurses reported slightly higher mean use at 30 percent, ranging from 5 percent in China and Australia to 60 percent in the United States. The LAIs most frequently reported included haloperidol (47 percent), paliperidone palmitate (47 percent), aripiprazole (35 percent), risperidone (29 percent), olanzapine (18 percent), and zuclopenthixol (12 percent).

When asked about their general approach to prescribing LAIs, 40% of psychiatrists described them as primarily for patients with adherence difficulties on oral medications ("adherence reserved"), 30 percent reported using LAIs as early as possible in treatment ("early LAI users"), and 30 percent reserved LAIs for patients with more severe symptoms or after other treatments failed ("severity reserved"). Among psychiatric nurses, 43% identified as "severity reserved," while 29% each identified as "adherence reserved" or "early LAI users."

There was no clear consensus among HCPs regarding the ideal patient profile for LAI treatment **(Figure 2).** Many HCPs felt that LAIs should be limited in younger patients or those with milder disease. Notably, two HCPs in Australia supported LAI use in younger patients with few acute episodes, one explaining, "LAIs keep them engaged in treatment long-term while figuring out housing, education, employment." Similarly, two HCPs in Canada advocated for LAI use in patients experiencing first-episode psychosis.

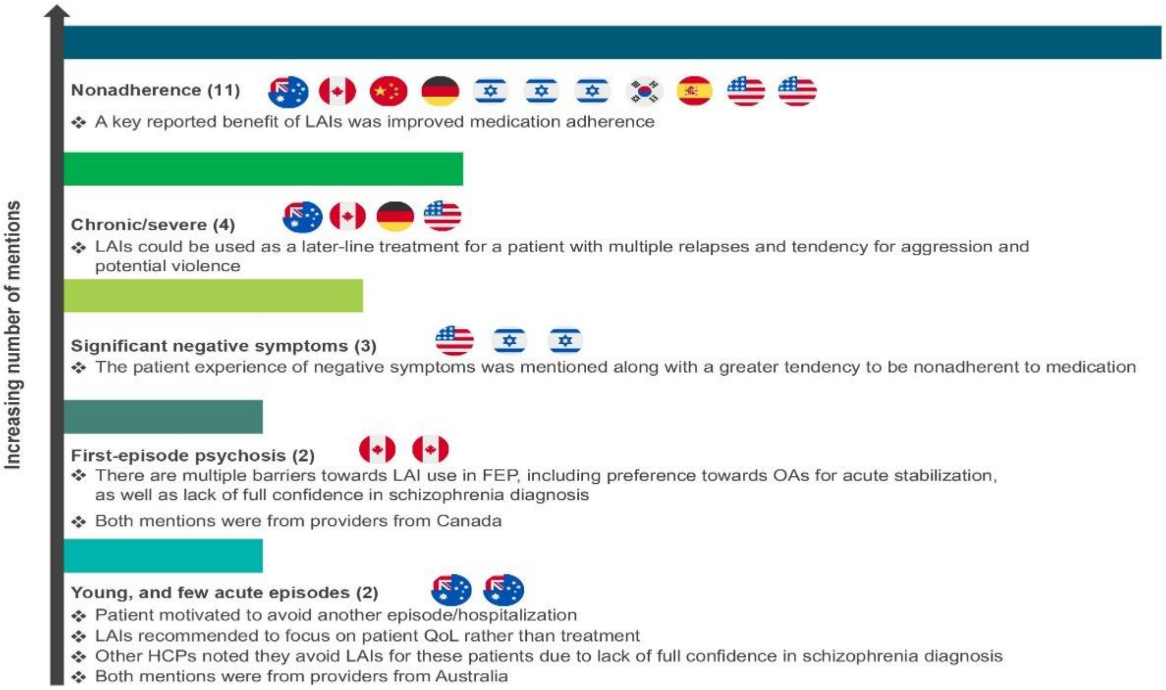


Figure 2. HCP Perspectives on patient profiles suitable for LAI treatment (Number of Mentions). FEP= first-episode psychosis; HCP= healthcare professional; LAI= long-acting injectable antipsychotic; OA= oral antipsychotic; QoL= quality of life. Flags indicate the country of the reporting HCP for each patient profile.

Challenges in LAI adoption

Psychiatrists highlighted several obstacles that can hinder the use of LAIs: fear or dislike of injections among patients (70%), difficulties in arranging or accessing treatment (60%), prior traumatic experiences with compulsory injections (50%), treatment costs (40%), concerns about loss of autonomy (30%), and stigma associated with LAI use (30%). Psychiatric nurses most frequently mentioned patient trauma from previous forced injections (43%) and logistical barriers (43%), followed by limited availability of certain LAI medications (29%), cost issues (14%), injection aversion (14%), and stigma (14%). Some nurses also reported negative experiences related to administering injections themselves.

Limited LAI availability was particularly noted in South Korea and China, where only a few formulations (one to three) are accessible. In China, financial cost emerged as a significant barrier affecting adoption.

Patient participants

Demographic and clinical characteristics

Out of 509 potential participants initially contacted, eighty patients responded to the outreach and underwent screening. Forty-two were invited for interviews, and 20 completed the full session. On average, participants were diagnosed with schizophrenia at 27 years of age, had been living with the disorder for approximately 11 years, and 60% were female **(Table 2)**. Regarding employment and living situations, 60% were either unemployed or receiving disability support, while 35% lived independently. Most patients (90%) received their initial diagnosis in an inpatient setting, while 10% were diagnosed in the community by a psychiatrist at a younger age.

Table 2. Demographic and clinical characteristics of patients (N = 20)

Country	Sex	Duration of Illness (years)	Age at Diagnosis (years)	Caregiver Relationship	Employment Status	Current/Previous LAI Use (Type)
Australia	Male	18	17	None	Receiving disability	Past LAI (risperidone, flupentixol)
	Male	5	50	None	Receiving disability	Current LAI (paliperidone)
	Female	3	34	Spouse	Unemployed	Current LAI (not specified)
	Female	16	27	None	Receiving disability	Past LAI (not specified)
Canada	Female	12	45	Child	Employed	Current LAI (paliperidone)
China	Female	19	27	Parent	Receiving disability	Never used LAIs
	Female	5	33	Parent	Student	Current LAI (olanzapine)
	Female	6	13	Parent	Receiving disability	Past LAI (not specified)
	Male	3	33	Parent	Receiving disability	Past LAI (not specified)
Germany	Male	13	25	None	Unemployed	Current LAI (haloperidol)
Israel	Female	13	19	None	Employed	Past LAI (olanzapine)
	Male	7	28	None	Employed	Current LAI (zuclopenthixol)
	Male	19	26	None	Employed	Current LAI (zuclopenthixol)
	Male	20	37	None	Employed	Past LAI (haloperidol, paliperidone)
South Korea	Female	15	25	None	Unemployed	Current LAI (not specified)
	Female	10	28	None	Unemployed	Current LAI (not specified)
	Female	8	28	Parent	Unemployed	Current LAI (not specified)
	Male	21	19	Spouse	Receiving disability	Current LAI (not specified)
Spain	Female	5	20	Parent	Student	Current LAI (paliperidone; past: aripiprazole)
United States	Female	5	20	Parent	Student	Current LAI (fluphenazine; past: paliperidone)

Patients most frequently identified social goals (n = 9) and employment-related objectives (n = 7) as their primary treatment priorities. Other goals included minimizing medication side effects (n = 3), improving daily functioning (n = 3), controlling positive symptoms (n = 2), and pursuing educational achievements (n = 2).

Treatment history

Among patients who could recall the specific antipsychotic they were first prescribed at the time of their schizophrenia diagnosis (n = 18; 90%), the majority (n = 17) had started on oral antipsychotics (OAs), while one patient received an LAI. Quetiapine and aripiprazole were the most frequently reported initial oral treatments. Currently, 65% of patients were receiving LAI therapy, and 35 percent (n = 7) had previous experience with LAIs. Among the various LAIs reported, paliperidone LAI was the most commonly mentioned (n = 3).

In most cases (90%), LAIs were first recommended by the patient's physician, and the initial introduction often occurred during an inpatient stay (70%). Patients emphasized the importance of continuity of care with a trusted healthcare professional who understands their individual needs and can tailor treatment accordingly.

Two distinct patterns of treatment and disease management emerged. Patients who were diagnosed early in the course of symptom development and received strong outpatient support, often with little or no hospitalization, tended to favor LAIs over oral medications (**Figure 3**, Profile 1). In contrast, patients who initially presented with severe acute episodes requiring hospitalization were more likely to decline LAI treatment in favor of oral therapy (**Figure 3**, Profile 2).

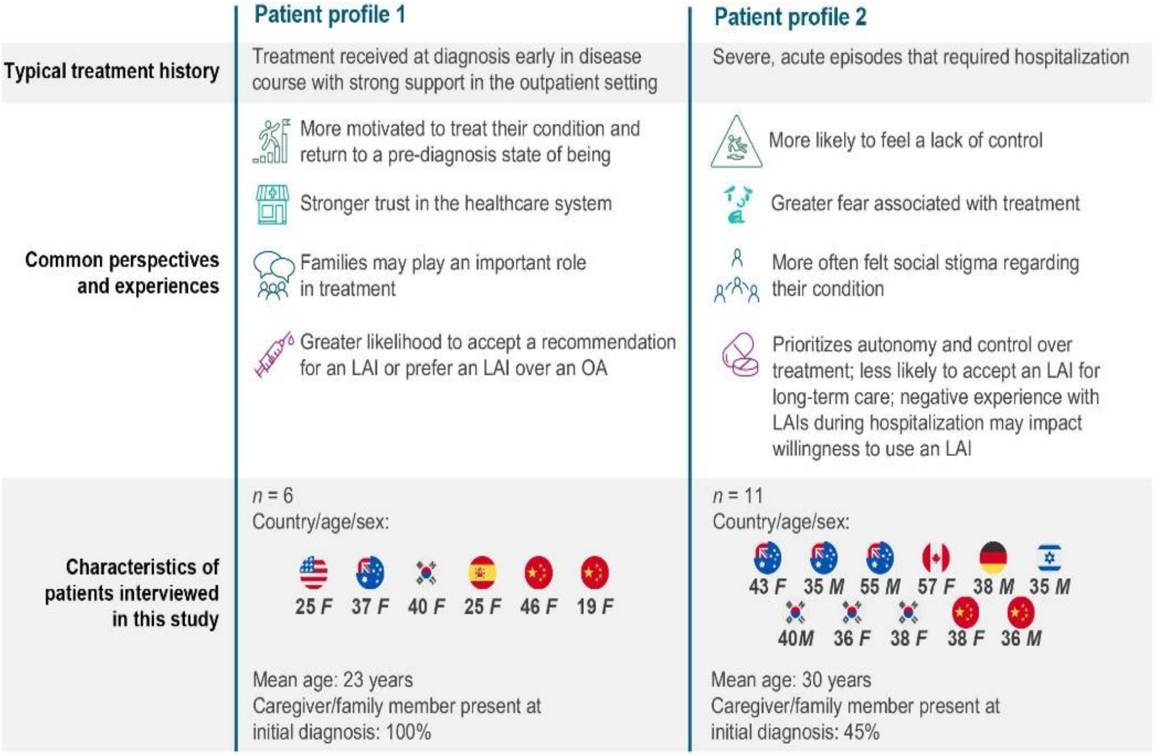
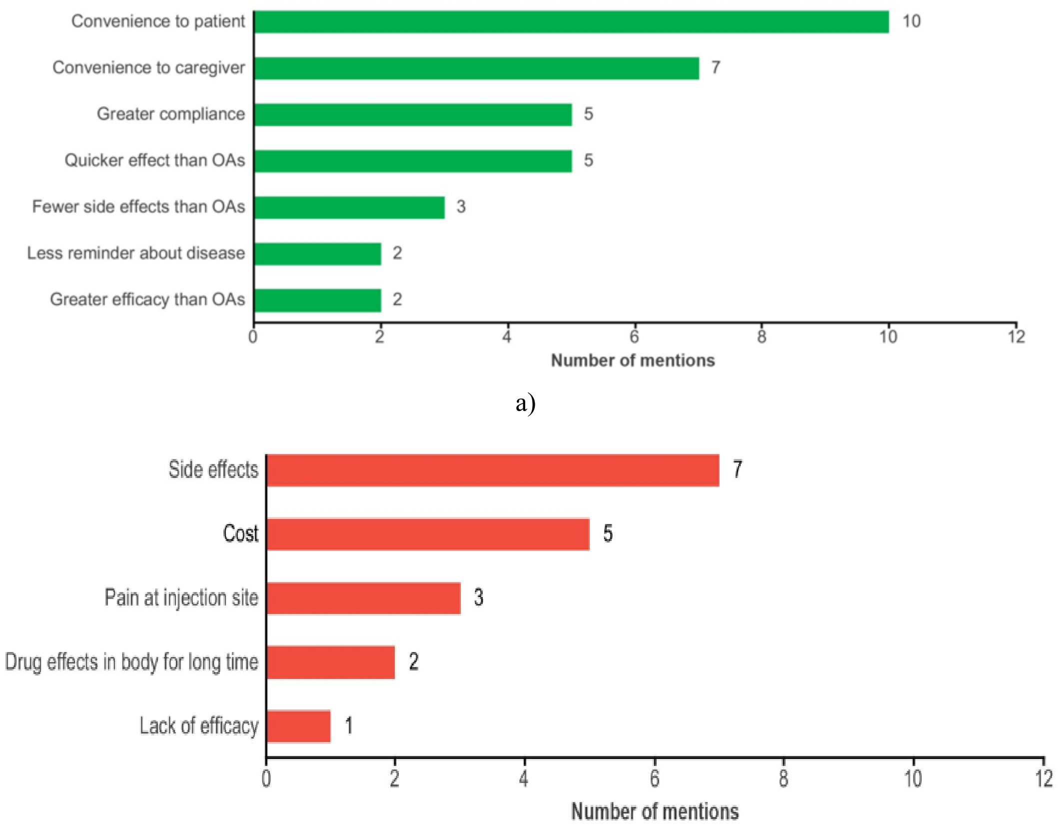


Figure 3. Two distinct patient profiles for schizophrenia. F= female; LAI= long-acting injectable antipsychotic; M= male; OA= oral antipsychotic.

Patient perspectives on LAIs

Patients most frequently identified convenience (n = 7) as the primary benefit of LAI treatment, followed by experiencing fewer side effects compared with oral antipsychotics (n = 3). Additional advantages noted included more stable symptom control with fewer fluctuations (n = 1), improved overall treatment effectiveness (n = 1), and a faster onset of therapeutic effects (n = 1) relative to oral medications **(Figure 4a).**



a)

b)

Figure 4. Patient perspectives on LAIs: (a) Reported Benefits and (b) Reported Concerns. LAI= long-acting injectable antipsychotic; OA= oral antipsychotic.

The primary drawbacks mentioned regarding LAIs included discomfort from the injection site (reported by 3 participants) and adverse reactions (also by 3 participants). Additional worries involved financial burden (2 participants), potential aggravation of negative symptoms (2 participants), prolonged presence of the medication in the system (1 participant), and possibility of symptom recurrence when transitioning treatments (1 participant) (**Figure 4b**). The two individuals who raised issues about affordability resided in Israel and South Korea. One individual noted that financial constraints prevented them from accessing an LAI.

Caregivers

Demographics of participants

Of the 34 caregivers initially evaluated, 23 were selected for involvement, and 19 successfully finished the complete interview process. Among those interviewed, 74% were either relatives or partners of the individual diagnosed with schizophrenia. The average duration of caregiving for the person with schizophrenia was seven years; specifically, 21% had provided support for fewer than 5 years, 58% for 5 to 10 years, and 21 percent for more than 10 years **(Table 3).**

Table 3. Demographic and caregiving characteristics of participants (N = 19)

Country	Relationship to Patient	Duration of Care (years)	Patient's LAI Status
Australia	Friend	8	Currently receiving LAI
	Sibling	5	Currently receiving LAI
	Parent	5	Previously received LAI
	Spouse	7	Currently receiving LAI
Canada	Professional	3	Currently receiving LAI
China	Sibling	3	Never received LAIs

	Child	7	Currently receiving LAI
	Parent	10	Previously received LAI
	Parent	6	Previously received LAI
Germany	Parent	20	Previously received LAI
Israel	Parent	6	Previously received LAI
	Spouse	14	Currently receiving LAI
	Professional	8	Previously received LAI
South Korea	Spouse	30	Currently receiving LAI
	Sibling	10	Currently receiving LAI
	Professional	2	Currently receiving LAI
	Professional	3	Currently receiving LAI
Spain	Parent	23	Currently receiving LAI
United States	Child	8	Never received LAIs

More than half of caregivers (53 percent; n = 10) supported individuals who were initially diagnosed with schizophrenia during an inpatient stay. The presence of caregivers at the time of diagnosis varied depending on their relationship with the person living with schizophrenia. Among those who were present at diagnosis (60 percent; n = 6), half were parents (30%) and half were siblings (30%).

Caregiver–patient relationships often evolved over time. Six of nine caregivers (67%; including five who were children, siblings, or friends) described improvements and strengthened bonds as the relationship developed. In contrast, three of nine caregivers (33%; two parents and one spouse) reported persistent conflict, which negatively affected the relationship.

Roles of caregivers

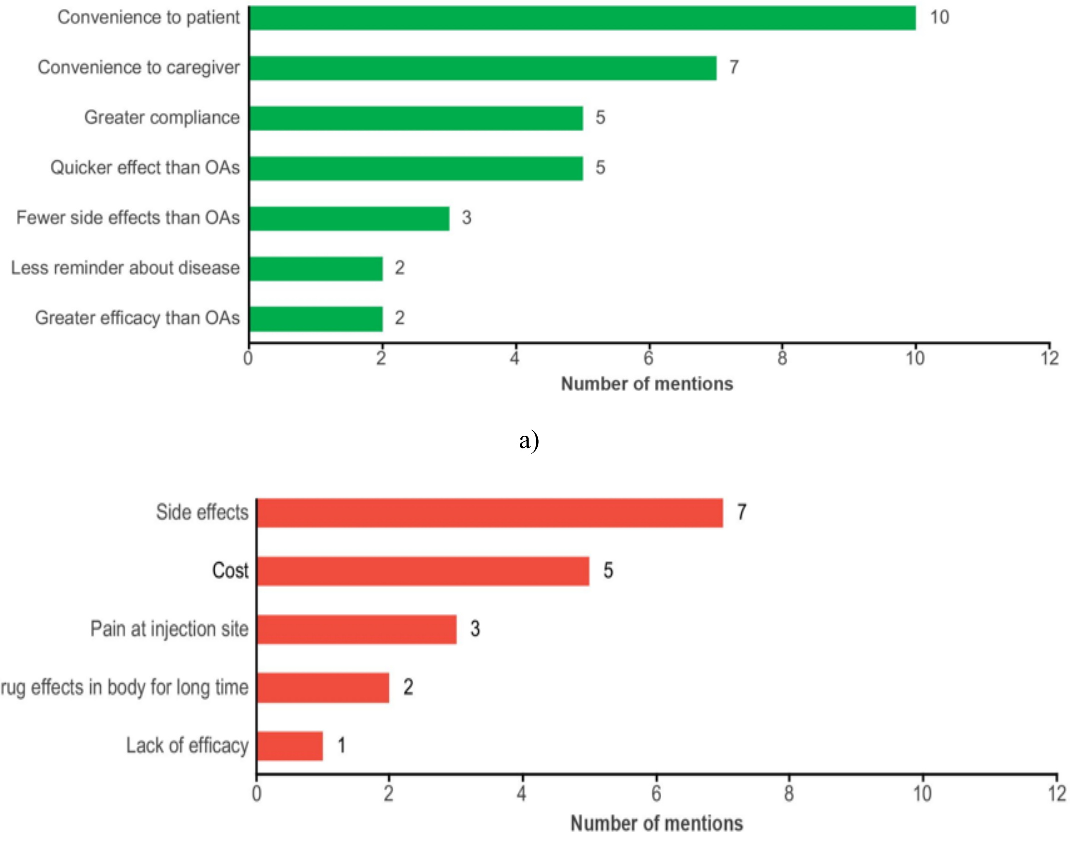
Caregivers took on diverse responsibilities, including reminding patients to take medications, providing transportation to appointments, monitoring and communicating side effects, initiating discussions about treatment, and offering emotional, financial, and practical support.

In treatment decision-making, 21% of caregivers described themselves as somewhat involved, 42% as involved, 26% as very involved, and 11% as the primary decision-maker for the patient. Across decisions, caregivers prioritized both the patient's quality of life and symptom management.

Caregiver views on LAIs

Among patients under their care, 58 percent (n = 11) were currently using an LAI, while 32 percent (n = 6) had used one in the past. Nearly all caregivers (95%) reported that the patient's physician initiated discussions about LAI treatment. One caregiver noted having introduced the LAI topic themselves after learning about it from other patients in the hospital. Most caregivers (89%) were unfamiliar with LAIs prior to the initial conversation with the healthcare provider.

Caregivers highlighted several perceived benefits of LAIs. Convenience for the patient (53 percent) and for the caregiver (37%) were most frequently mentioned. Additional benefits included improved adherence (26%), faster onset of effect compared with oral medications (26%), reduced side effects (16 percent), fewer daily reminders of illness (11%), and higher treatment efficacy than oral antipsychotics (11%) **(Figure 5a).** One caregiver summarized the convenience, stating, "With the injections, they don't have to think about it. Daily pills are a reminder that they are not doing well."



a)

b)

Figure 5. Caregiver-reported perceptions of LAIs: (a) reported benefits and (b) reported concerns. LAI, long-acting injectable antipsychotic; OA, oral antipsychotic.

The primary concerns caregivers reported regarding LAI therapy were side effects (37 percent) and treatment cost (26 percent). Additional concerns included pain at the injection site (16 percent), prolonged drug presence in the body (11 percent), and doubts about efficacy (5 percent) **(Figure 5b).** Side effect concerns were often linked to insufficient information and education about LAIs. Caregivers who cited cost as a barrier were located in Israel (n = 2), China (n = 2), and Canada (n = 1).

Caregiver-reported unmet needs

The most frequently reported unmet need among caregivers was more comprehensive educational resources about treatment options for schizophrenia (32%). Many caregivers indicated that they had not received adequate guidance from the patients' healthcare providers and had to independently seek information to understand optimal treatment approaches. Other reported needs included access to caregiver support groups (16%), mental health or wellness support for the caregiver (16%), and faster access to healthcare professionals (5%).

This multinational qualitative study of healthcare professionals, patients with schizophrenia, and caregivers offers insight into treatment goals and experiences with LAIs from multiple perspectives, helping to explain international differences in LAI utilization. Key strengths of the study include its global sampling strategy and the use of semi-structured interview guides developed based on existing evidence regarding barriers and facilitators to LAI adoption. Another strength lies in capturing the views of the three primary stakeholders in schizophrenia care: patients, caregivers, and clinicians. The findings provide valuable guidance for managing schizophrenia in diverse healthcare settings and have informed a conceptual model of the patient journey from diagnosis to treatment selection and ongoing monitoring **(Figure 6).**

Additionally, these insights have important implications for shaping health policy related to schizophrenia care.

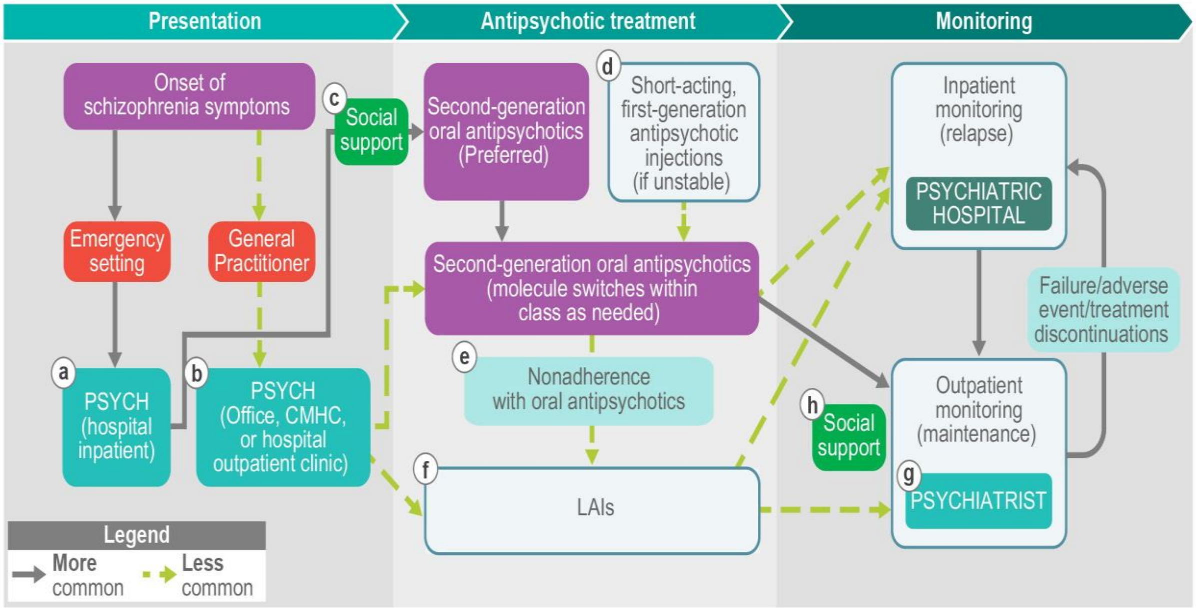


Figure 6. Conceptual pathway from schizophrenia symptom onset to treatment and follow-up. CMHC, community mental health center; HCP, healthcare professional; LAI, long-acting injectable antipsychotic; psych, psychiatrist. (a) Experiences during inpatient hospitalization may lead patients to associate LAIs with loss of autonomy or physical discomfort, or foster a general mistrust of HCPs. (b) Patients who engage with outpatient care early may have more influence over treatment decisions and be more likely to receive LAI recommendations. (c) Strong social support may increase both the likelihood that HCPs recommend LAIs and that patients accept them. (d) Individuals with a prior history of coerced injections in hospitals may hold negative views toward LAIs and resist recommendations. (e) Patients who try LAIs after previously being nonadherent to oral medications may also develop negative perceptions. (f) Patients first offered LAIs in outpatient settings tend to perceive them more positively. (g) Support from family, caregivers, or social workers can encourage continued treatment by highlighting benefits. (h) Greater trust in outpatient HCPs is associated with more favorable views of LAIs.

HCP participants

HCPs identified several factors shaping their attitudes toward LAIs, including availability, cost, side effect profiles, patient preferences, and care settings. Psychiatrists, particularly in inpatient contexts, prioritized managing positive symptoms first, followed by improving patient quality of life (QoL). In contrast, psychiatric nurses emphasized QoL as the primary goal, possibly reflecting their closer, more frequent interactions with patients and deeper understanding of daily challenges. Overall, HCPs expressed generally positive views on LAIs and recognized potential benefits for both patients and clinicians, but many reserved LAIs for patients with poor adherence to oral medications. Key barriers reported included patient aversion to injections, logistical limitations (e.g., staffing, training), and product availability and cost.

These findings align with previous research. For example, a survey of 379 HCPs indicated reluctance to discuss LAIs with patients who are adherent to oral antipsychotics [24]. Similarly, the PRELAPSE study found that despite favorable opinions of LAIs, HCPs primarily focused on their use in nonadherent patients and hesitated to recommend them to younger individuals [14]. This hesitation persists despite evidence showing benefits of early LAI use, such as reduced relapse risk [25], better symptom control [26], and lower treatment costs, including hospitalization and outpatient visits [27]. While some HCPs initiate LAIs early, overall usage remains suboptimal [13].

Delays in LAI initiation suggest a knowledge gap that could be addressed through targeted education on the advantages of earlier LAI use. Systemic barriers, such as cost and product availability, remain difficult to overcome, but perceptual barriers—like assumptions that patients will reject injections—can be mitigated through HCP education and early discussions about patient treatment preferences. Psychiatric nurses also reported limited knowledge of specific LAI formulations, indicating the need for more focused training.

Patient and caregiver participants

Patients' experiences across their treatment journey highlighted key factors shaping LAI perceptions **(Figure 6)**. Interactions with HCPs, family support, previous hospitalizations, and logistical considerations (e.g., travel to injection clinics) all influence views on LAIs. The treatment setting emerged as particularly influential: in Australia, Canada, Germany, and Israel, patients reported that inpatient treatment discussions were dominated by psychiatrists, leaving patients with minimal autonomy. Patients who received LAIs during acute inpatient episodes—especially as forced or court-ordered injections—may associate LAIs with pain and loss of control, creating barriers to future acceptance and preference for oral medications. Other factors, such as active paranoia or prior positive experience with oral clozapine for treatment-resistant schizophrenia, also shape LAI acceptance. Conversely, patients engaged in outpatient care early are more likely to participate in treatment decisions, trust their HCPs, and discuss QoL considerations, generally resulting in more positive perceptions of LAIs.

During the maintenance and monitoring phase, support networks influence treatment engagement. Patients with strong backing from family, caregivers, social workers, or case managers are more likely to adhere to treatment, as improvements in outcomes, such as psychotic symptoms, become apparent. Caregivers emphasized the importance of shifting focus from symptom control to recovery and QoL to help patients regain meaningful activities. This study underscores the crucial role caregivers play in treatment decisions, especially in outpatient contexts or post-hospitalization, by promoting communication—a factor particularly important for patients with limited insight, low motivation, or mistrust of clinicians.

Participants in this study identified convenience and a lower incidence of side effects as primary advantages of LAIs compared with oral antipsychotics (OAs), although concerns about potential side effects persisted. Caregivers also recognized multiple benefits of LAIs for themselves and the individuals they support, including ease of administration, improved adherence, faster therapeutic effects, fewer adverse effects, reduced reminders of illness, and a decreased frequency of treatment-related discussions. The presence of a caregiver or broader social support network may further increase the likelihood that HCPs recommend LAIs and that patients accept them. However, caregivers highlighted the need for enhanced education and discussion regarding treatment options, including effectively communicating the practical benefits of LAIs to those under their care.

The interplay between patient treatment experiences and perceptions of interventions such as LAIs, observed in this study, aligns with existing literature. Individuals with schizophrenia often experience cyclical patterns of relapse and maintenance, involving repeated interactions with both inpatient and outpatient care systems and HCPs [28]. Symptom presentation and the initial context of diagnosis and treatment can vary, influenced by demographic, systemic, and disease-specific factors. Systemic constraints, such as psychiatrist availability and treatment costs, may result in patients receiving care in inpatient settings [10]. In countries with limited outpatient psychiatric resources—such as Australia, Canada, Germany, and Israel in this study—patients may rely more on general practitioners, who may have limited capacity to manage schizophrenia optimally.

Consistent with prior research, a robust support system combined with behavioral interventions can enhance medication adherence [29]. Our results correspond with a qualitative US study (N = 16) involving semi-structured interviews with HCPs, patients, and caregivers, which emphasized that collaborative relationships and a treatment culture that respects patient autonomy are key drivers of LAI acceptance [30]. Similarly, the STAR NETWORK Depot Study in Italy (N = 451), a multicenter longitudinal observational study, identified improved patient engagement with outpatient psychiatric services as the primary reason for LAI prescription and adherence [31]. In a US non-randomized study of 60 HCPs analyzing recorded patient interactions, patients were more likely to accept LAIs when HCPs highlighted the benefits of newer LAIs or superior therapeutic outcomes compared with OAs [32]. Moreover, caregivers in the present study stressed the importance of prioritizing recovery and quality of life (QoL) alongside symptom management, a perspective supported by a study of 253 patient-caregiver pairs in Bolivia, Chile, and Peru, which found a positive association between patients' QoL, severity of psychotic symptoms, and caregivers' QoL [33].

Educating patients on the safety profile of LAIs and preparing them for potential injection-site reactions may enhance acceptance of LAI recommendations. These findings underscore the importance of making patient and family education on treatments, including LAIs, practical, accessible, and available in both inpatient and outpatient contexts. Effective approaches may include peer educators or peer specialists who have lived experience to facilitate informed decision-making, as well as family-centered psychotherapeutic and care coordination strategies [34, 35]. From a health policy perspective, ensuring access to specialized psychiatric care and support early in the schizophrenia recovery trajectory may help mitigate downstream complications experienced by a significant proportion of patients and their families.

Limitations

The qualitative interviews in the ADVANCE study aimed to capture a comprehensive understanding of the perspectives of those involved in the care of individuals living with schizophrenia. Nevertheless, qualitative research inherently has certain limitations. Due to the intensive and detailed nature of the interviews, each participant group was relatively small, and only a limited number of healthcare professionals (HCPs) represented each country, restricting the representativeness of country-specific findings. Including participants from multiple countries provided valuable insight into experiences across different regions; however, variations in local treatment guidelines, healthcare systems, and clinical practices introduced heterogeneity. Combined with the small sample size and potential selection bias, this may constrain the generalizability of some results. Despite this, the use of diverse social, digital, and professional recruitment channels, along with the alignment of participants' backgrounds with the study's objectives, offers reasonable confidence that these findings are relevant to the broader population of HCPs, patients with schizophrenia, and caregivers.

This study did not include psychologists or psychotherapists; given their close therapeutic relationships with patients, future research incorporating these professionals could provide additional perspectives affecting LAI utilization. Because all participants had prior experience with LAIs, the findings may not fully reflect the views of those caring for individuals with schizophrenia who have not used or been recommended LAIs. Information on the type of current or previous LAI treatment was not available for all patients, and treatment dosages were not collected in this study. More detailed drug-related data were gathered in the quantitative component of ADVANCE, which will be reported separately. Triads consisting of a patient, their caregiver, and their HCP were not included due to the difficulty of identifying such groupings. Finally, as with any survey-based study, the results may be influenced by recall bias and the potential for participants to misinterpret interview questions.

Conclusion

Interactions between patients and psychiatrists or psychiatric nurses differ across care settings, which can affect the acceptance and use of LAIs. Treatment goals reported by HCPs varied depending on the care environment, with inpatient care primarily focused on stabilizing or managing positive symptoms, while outpatient care emphasized improving patient quality of life (QoL). HCP attitudes toward LAIs were shaped by factors including drug availability, side effect profiles, patient preferences, and HCP perceptions of patient preferences. There remains no clear consensus on the ideal patient profile for LAI use; most interviewed HCPs suggested limiting LAIs in younger patients or those with less severe symptoms, although evidence indicates that early use of LAIs and use in younger patients may offer clinical benefits.

Several factors along the patient journey—from symptom onset to diagnosis and treatment initiation—may influence whether a patient is recommended or accepts an LAI. These include the initial care setting, family support, hospitalizations, trust in HCPs, and logistical challenges, all of which can affect patient outcomes and perceptions of LAIs. Patients and caregivers generally recognize the advantages of LAIs but express concerns regarding side effects. In outpatient settings, families and caregivers play a crucial role in bridging gaps for patients with limited insight, motivation, or trust in HCPs, facilitating access to treatment options such as LAIs. The study found that most caregivers were initially unaware of LAIs, indicating a need for educational resources to support discussions among HCPs, patients, and caregivers. Targeted education addressing the specific concerns of each group may help reduce barriers to LAI adoption.

Acknowledgments: None

Conflict of Interest: None

Financial Support: None

Ethics Statement: None

References

1. Kadakia A, Catillon M, Fan Q, Williams GR, Marden JR, Anderson A, et al. The economic burden of schizophrenia in the United States. *J Clin Psychiatry*. (2022) 83:22m14458. doi: 10.4088/JCP.22m14458
2. Wei Y, Yan VKC, Kang W, Wong ICK, Castle DJ, Gao L, et al. Association of long-acting injectable antipsychotics and oral antipsychotics with disease relapse, health care use, and adverse events among people with schizophrenia. *JAMA Network Open*. (2022) 5:e2224163. doi: 10.1001/jamanetworkopen.2022.24163
3. Solmi M, Seitidis G, Mavridis D, Correll CU, Dragioti E, Guimond S, et al. Incidence, prevalence, and global burden of schizophrenia - data, with critical appraisal, from the global burden of disease (Gbd) 2019. *Mol Psychiatry*. (2023) 28:5319–27. doi: 10.1038/s41380-023-02138-4
4. He H, Liu Q, Li N, Guo L, Gao F, Bai L, et al. Trends in the incidence and dalys of schizophrenia at the global, regional and national levels: results from the global burden of disease study 2017. *Epidemiol Psychiatr Sci*. (2020) 29:e91. doi: 10.1017/S2045796019000891
5. Crespo-Facorro B, Such P, Nylander AG, Madera J, Resemann HK, Worthington E, et al. The burden of disease in early schizophrenia - a systematic literature review. *Curr Med Res Opin*. (2021) 37:109–21. doi: 10.1080/03007995.2020.1841618
6. Emsley R, Chiliza B, Asmal L, and Harvey BH. The nature of relapse in schizophrenia. *BMC Psychiatry*. (2013) 13:50. doi: 10.1186/1471-244X-13-50
7. Kamil SH and Velligan DI. Caregivers of individuals with schizophrenia: who are they and what are their challenges? *Curr Opin Psychiatry*. (2019) 32:157–63. doi: 10.1097/yco.0000000000000492
8. Shamsaei F, Cheraghi F, and Bashirian S. Burden on family caregivers caring for patients with schizophrenia. *Iran J Psychiatry*. (2015) 10:239–45.
9. Haddad PM, Brain C, and Scott J. Nonadherence with antipsychotic medication in schizophrenia: challenges and management strategies. *Pat Related Outcome Measures*. (2014) 5:43–62. doi: 10.2147/PROM.S42735
10. Schwartz S, Carilli C, Mian T, Ruekert L, and Kumar A. Attitudes and perceptions about the use of long-acting injectable antipsychotics among behavioral health practitioners. *Ment Health Clinic*. (2022) 12:232–40. doi: 10.9740/mhc.2022.08.232
11. Faden J, Ramirez C, Martinez V, and Citrome L. An overview of the currently available and emerging long-acting formulations of risperidone for schizophrenia and bipolar disorder. *Expert Rev Neurother*. (2024) 24:761–71. doi: 10.1080/14737175.2024.2370349
12. Markowicz-Piasecka M, Kubisiak M, Asendrych-Wicik K, Kolodziejczyk M, Grzelinska J, Fabijanska M, et al. Long-acting injectable antipsychotics-a review on formulation and *in vitro* dissolution. *Pharmaceutics*. (2023) 16:28. doi: 10.3390/pharmaceutics16010028
13. Correll CU, Citrome L, Haddad PM, Lauriello J, Olfson M, Calloway SM, et al. The use of long-acting injectable antipsychotics in schizophrenia: evaluating the evidence. *J Clin Psychiatry*. (2016) 77:1–24. doi: 10.4088/JCP.15032su1
14. Kane JM, Schooler NR, Marcy P, Correll CU, Achtyes ED, Gibbons RD, et al. Effect of long-acting injectable antipsychotics vs usual care on time to first hospitalization in early-phase schizophrenia: A randomized clinical trial. *JAMA Psychiatry*. (2020) 77:1217–24. doi: 10.1001/jamapsychiatry.2020.2076
15. Patel MX, Bent-Ennakhil N, Sapin C, di Nicola S, Loze JY, Nylander AG, et al. Attitudes of european physicians towards the use of long-acting injectable antipsychotics. *BMC Psychiatry*. (2020) 20:123. doi: 10.1186/s12888-020-02530-2
16. Velligan D, Salinas GD, Belcher E, Frazenburg KR, Suett M, Thompson S, et al. (2022). Differences between high and low users of long-acting injectable antipsychotics for patients with schizophrenia: A

survey of us-practicing psychiatric clinicians, in: Annual NEI Psychopharmacology Congress, Colorado Springs, Colorado, USA.

17. Cahling L, Berntsson A, Bröms G, and Öhrmalm L. Perceptions and knowledge of antipsychotics among mental health professionals and patients. *BJPsych Bull*. (2017) 41:254–9. doi: 10.1192/pb.bp.116.055483
18. Fitzgerald HM, Shepherd J, Bailey H, Berry M, Wright J, and Chen M. Treatment goals in schizophrenia: A real-world survey of patients, psychiatrists, and caregivers in the United States, with an analysis of current treatment (Long-acting injectable vs oral antipsychotics) and goal selection. *Neuropsychiatr Dis Treat*. (2021) 17:3215–28. doi: 10.2147/ndt.S330936
19. Keenan A, Lin D, Shepherd J, Bailey H, Benson C, and Meakin S. Patient-psychiatrist discordance and drivers of prescribing long-acting injectable antipsychotics for schizophrenia management in the real-world: A point-in-time survey. *BMC Psychiatry*. (2022) 22:187. doi: 10.1186/s12888-022-03846-x
20. Agid O, Remington G, Fung C, Nightingale NM, Duclos M, and Anger GJ. Real-world utilization patterns of long-acting injectable antipsychotics in Canada: A retrospective study. *Can J Psychiatry Rev Can Psychiatr*. (2022) 67:226–34. doi: 10.1177/07067437211055413
21. Oguchi Y, Miyake N, and Ando K. Barriers to long-acting injectable atypical antipsychotic use in Japan: insights from a comparative psychiatrist survey. *Neuropsychopharmacol Rep*. (2024) 44:417–23. doi: 10.1002/npr2.12435
22. Frazenburg KR, Hansen RT, Suett M, Yaari A, Levin AP, Sergerie M, et al. *Attitudes driving regional differences in lai antipsychotic utilization for schizophrenia among healthcare profesionals, patients, and caregivers (Advance): patient and caregiver qualitative interviews*. (2024), In press.
23. Frazenburg KR, Hansen RT, Suett M, Yaari A, Levin AP, Sergerie M, et al. *Attitudes driving regional differences in long-acting injectable antipsychotic (Lai) antipsychotic utilization for schizophrenia among healthcare professionals, patients, and caregivers (Advance): healthcare professional qualitative interviews*. (2024), In press.
24. Citrome L, Belcher E, Stacy S, Suett M, Mychaskiw M, and Salinas GD. Management of schizophrenia with long-acting injectable antipsychotic medications: an assessment of the educational needs of clinicians. *Neuropsychiatr Dis Treat*. (2022) 18:111–23. doi: 10.2147/ndt.S326299
25. Kim B, Lee SH, Choi TK, Suh S, Kim YW, Lee E, et al. Effectiveness of risperidone long-acting injection in first-episode schizophrenia: in naturalistic setting. *Prog Neuropsychopharmacol Biol Psychiatry*. (2008) 32:1231–5. doi: 10.1016/j.pnpbp.2008.03.012
26. Stevens GL, Dawson G, and Zummo J. Clinical benefits and impact of early use of long-acting injectable antipsychotics for schizophrenia. *Early Interven Psychiatry*. (2016) 10:365–77. doi: 10.1111/eip.12278
27. Kane JM, Peters-Strickland T, Baker RA, Hertel P, Eramo A, Jin N, et al. Aripiprazole once-monthly in the acute treatment of schizophrenia: findings from a 12-week, randomized, double-blind, placebo-controlled study. *J Clin Psychiatry*. (2014) 75:1254–60. doi: 10.4088/JCP.14m09168
28. Patel KR, Cherian J, Gohil K, and Atkinson D. Schizophrenia: overview and treatment options. *P T: peer-reviewed J Formul Manage*. (2014) 39:638–45.
29. Phan SV. Medication adherence in patients with schizophrenia. *Int J Psychiatry Med*. (2016) 51:211–9. doi: 10.1177/0091217416636601
30. Carroll AJ, Robinson DG, Kane JM, Kordon A, Bannon J, Walunas TL, et al. Multi-level barriers and facilitators to implementing evidence-based antipsychotics in the treatment of early-phase schizophrenia. *Front Health Serv*. (2024) 4:1385398. doi: 10.3389/frhs.2024.1385398
31. Barbui C, Bertolini F, Bartoli F, Calandra C, Callegari C, Carrà G, et al. Reasons for initiating long-acting antipsychotics in psychiatric practice: findings from the star network depot study. *Ther Adv Psychopharmacol*. (2020) 10:2045125320978102. doi: 10.1177/2045125320978102
32. Potkin S, Bera R, Zubek D, and Lau G. Patient and prescriber perspectives on long-acting injectable (Lai) antipsychotics and analysis of in-office discussion regarding lai treatment for schizophrenia. *BMC Psychiatry*. (2013) 13:261. doi: 10.1186/1471-244X-13-261
33. Caqueo-Urízar A, Alessandrini M, Urzúa A, Zendjidjian X, Boyer L, and Williams DR. Caregiver's quality of life and its positive impact on symptomatology and quality of life of patients with

schizophrenia. *Health Qual Life Outcomes*. (2017) 15:76. doi: 10.1186/s12955-017-0652-6

34. Jambawo SM, Owolewa R, and Jambawo TT. The effectiveness of peer support on the recovery and empowerment of people with schizophrenia: A systematic review and meta-analysis. *Schizophr Res*. (2024) 274:270–9. doi: 10.1016/j.schres.2024.10.006
35. Caqueo-Urizar A, Rus-Calafell M, Urzua A, Escudero J, and Gutierrez-Maldonado J. The role of family therapy in the management of schizophrenia: challenges and solutions. *Neuropsychiatr Dis Treat*. (2015) 11:145–51. doi: 10.2147/NDT.S51331
36. Association EPHMRA. *2024 ephmra code of conduct*. Basel, Switzerland: European Pharmaceutical Marketing Research Association (2024).