

Exploring Patient, Caregiver, and Prescriber Preferences for an Injectable Antipsychotic Administered Every 2 Months for the Maintenance Treatment of Schizophrenia: A Multicenter Qualitative Interview Study Conducted in Europe

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Purpose: This qualitative study explored patient, caregiver, and prescriber preferences for long-acting injectable (LAI) dosing frequency, and factors influencing preferences for a hypothetical LAI administered once every 2 months for the treatment of schizophrenia.

Patient and Methods: This single-person interview study recruited people living with schizophrenia, caregivers, and prescribers across France, Germany, Italy, Spain, and the UK. Semi-structured interviews were conducted in which participants were asked about their treatment experiences, views on an ideal treatment, and preferences on LAI dosing frequency. A qualitative analysis of interview transcripts was performed to identify key themes.

Results: Fifteen people living with clinically stable schizophrenia, 11 caregivers, and 13 prescribers were interviewed. When talking about current treatment (a once-monthly LAI), people living with schizophrenia and caregivers expressed mixed views, with some describing treatment as “easy”, whilst others described a fear that treatment will stop working or are frustrated with the frequency of appointments. When asked about treatment goals, a common theme was wishing for the person living with schizophrenia to be clinically stable, leading to a reduction in symptoms and emotional outbursts. When asked about an LAI administered once every 2 months, people living with schizophrenia and caregivers expressed positive views, and perceived that such a treatment would be less burdensome than current treatment. Prescribers were open to recommending an LAI given once every 2 months to clinically stable patients, or those expressing a preference for a decreased dosing frequency or for LAIs in general.

Conclusion: In this qualitative study, participants expressed overall positive views on a potential transition to an LAI given once every 2 months, due to the advantages of greater freedom and less treatment burden. Selection of a specific LAI should acknowledge individual patient and caregiver preferences regarding formulation and frequency, to ensure that targeted disease management goals are met.

Keywords: dosing frequency, long-acting injectable, healthcare professional preferences, patient preferences, caregiver preferences, shared decision-making

Introduction

Schizophrenia is a chronic and debilitating mental health disorder that is estimated to affect 23.6 million people worldwide.¹ It has a typical onset in late adolescence or early adulthood,¹ and is associated with significant morbidity and mortality that accrues a substantial clinical and economic burden to people living with schizophrenia and their caregivers, as well as to the healthcare systems, and society.^{2,3} Schizophrenia has a negative impact on levels of burden and stress experienced by caregivers and,⁴ in turn, this burden affects the health-related quality of life of those with schizophrenia.⁵

Maintenance treatment with antipsychotic therapy is recommended in schizophrenia to achieve and maintain symptom control and prevent relapse.^{6,7} However, adherence to oral antipsychotics is often poor, with an estimated 67% of patients not taking their treatment as prescribed.⁸ Non-adherence is associated with a significantly increased risk of relapse,⁹ which has been correlated with accelerated disease progression.¹⁰

Long-acting injectable (LAI) formulations of second-generation antipsychotics improve treatment adherence compared with daily oral treatments,¹¹ thus reducing the rate of relapse and hospitalization, protecting people living with schizophrenia from progressive functional decline,¹² and reducing mortality.^{13,14} In addition to their clinical benefits, LAIs offer improved convenience compared with daily oral therapies, and the introduction of LAIs with longer dosing intervals (ie, an interval longer than one month) may positively affect patients' subjective wellbeing, quality of life, and treatment satisfaction.^{15,16}

Despite the recognized benefits of LAIs, there is evidence that they are underutilized in people living with schizophrenia.^{2,17,18} While adherence is comparatively better with LAIs than with oral therapies,¹⁴ it may still be suboptimal due to interruptions in treatment and partial compliance.^{19–21} To improve adherence, it is important to understand factors affecting medication compliance in people living with schizophrenia, such as perceptions of the partnership with their prescriber,²² and factors influencing their willingness to try a new medication, such as treatment goals.²³ Consequently, physician assessment of patient views and concerns is an important aspect of shared decision-making,²⁴ and deriving a personalized treatment plan to support treatment continuation and improve satisfaction and outcomes.^{23,25}

Several studies have used surveys or questionnaires to investigate the views of people living with schizophrenia, caregivers, and healthcare professionals on the use of LAIs for the management of schizophrenia.^{25–31} Some of these preference studies focused on understanding perceptions of a specific LAI with a dosing interval longer than one month,^{25,26,28–30} with several studies gathering data in a clinical trial setting.^{25–27,31} These studies demonstrated that an antipsychotic treatment with a dosing interval longer than one month may have several benefits for people living with schizophrenia, as well as for their caregivers, including improved flexibility and convenience,^{29,30} reduced treatment burden and reduced caregiver burden,^{25,26,29} less stigmatization,^{28,30} reductions in the patient's focus on illness,²⁹ and increased involvement in daily activities and social interactions.^{28,29}

As the treatment landscape for schizophrenia continues to evolve, there is a need to improve our understanding of perceptions and preferences relating to disease management, and the potential role that LAIs with longer dosing intervals may play, beyond views relating to a specific treatment option. Therefore, this qualitative, single-person interview study takes a broader approach than previous studies and examines the personal perspectives of people living with schizophrenia, caregivers, and prescribers regarding treatment goals and LAI dosing frequency. Furthermore, the study (conducted in five countries across Europe) investigates preferences for a hypothetical LAI administered once every 2 months compared to an LAI given once monthly.

Materials and Methods

Study Objectives

The primary objective of the study was to explore the preferences of people living with schizophrenia regarding LAI features, including dosing frequency, and to identify factors that may influence preference for a hypothetical LAI administered once every 2 months. Secondary objectives were to understand the preferences of caregivers and prescribers with respect to LAI treatment features focusing on dosing frequency, identify factors that may influence the preference

for an LAI administered every 2 months, and examine similarities and differences in preferences between all three stakeholder groups.

An additional exploratory objective was to assess how caregivers and prescribers perceived the treatment preferences of people living with schizophrenia, and gain a better understanding of the experiences of shared decision-making during the discussion of treatment choices for all participants involved in the process.

Recruitment

This study planned to recruit people living with schizophrenia, caregivers, and prescribers across France, Germany, Italy, and Spain; during recruitment, the study was expanded to include the UK. Recruitment aimed to ensure variety across age and gender among people living with schizophrenia and caregivers, and variety across practice setting and specialties for prescribers. People living with schizophrenia and caregivers were recruited via a multimodal approach involving physician referral or other channels, such as panels, social media, patient advocacy groups, and recruitment partner databases. Prescribers were recruited through recruitment partner databases. The three groups of participants were independent of each other, such that people living with schizophrenia were not being cared for or treated by the caregivers or prescribers, respectively. Participants were required to self-report their eligibility criteria (Table 1), which were developed using patient-accessible language.

Study Materials

A review of the relevant scientific literature, public databases, and proprietary publications was conducted to identify key concepts relevant to preferences for different dosing regimen frequencies among people living with schizophrenia and their caregivers. These findings were used to inform the development of a semi-structured interview discussion guide for each participant group. Each of the discussion guides included the same core questions to harmonize the conversation flow across participant groups and countries. Interviews were conducted by moderators with experience of healthcare

Table 1 Key Eligibility Criteria for People Living With Schizophrenia, Caregivers, and Prescribers

Participant Group	Inclusion Criteria	Exclusion Criteria
People living with schizophrenia	Aged ≥ 18 years old Self-report of physician-diagnosed schizophrenia Currently treated with a once-monthly LAI Taking current antipsychotic medication for ≥ 3 months	Experience with a 2-, 3- or 6-month LAI Dual diagnosed with both bipolar I disorder and schizophrenia Currently experiencing an acute episode Currently being treated for their condition in the hospital setting Unable or unwilling to provide informed consent Member of, or immediate family member of, study personnel
Caregivers	Aged ≥ 18 years old Caregiver of a person living with schizophrenia meeting the study criteria Providing care and/or service to help manage the patient's health condition and life Visits or communicates with a person living with schizophrenia at least once a week	Paid for their caregiving duties Cares for a person living with schizophrenia who meets any of the exclusion criteria Member of, or immediate family member of, study personnel Caregiver of a person living with schizophrenia recruited to this study
Prescribers	Psychiatry as their main specialty Practicing for ≥ 3 years Spends $\geq 60\%$ of their time in direct patient care Manages ≥ 10 patients with schizophrenia in a typical month Prescribes LAI antipsychotics	Member of, or immediate family member of, study personnel Prescriber to a person living with schizophrenia recruited to this study

Abbreviation: LAI, long-acting injectable.

Table 2 Question Categories Included in the Semi-Structured Discussion Guide for Each Participant Group

Participant Group	Question Categories
People living with schizophrenia	Participant overview and background Views on an ideal treatment Schizophrenia treatment experience General views when deciding on a treatment Preferences on treatment frequency
Caregivers	Participant overview and background Views on an ideal treatment Current treatment regimen and impact General thoughts on treatment Preferences on treatment frequency
Prescribers	Participant overview and background Treating individuals with schizophrenia LAI perceptions and experience

Abbreviation: LAI, long-acting injectable.

research and training in qualitative methods. All moderators were given additional training in conducting interviews with vulnerable populations, including guidance and potential resources to share should participants experience distress during interviews. They were also all individually briefed on the study, including its goals and discussion guides. Some adaptations to the discussion guides were permitted, including the exact wording of questions, and the moderator could probe to explore topics further. The categories of questions that were included in the discussion guides are shown in Table 2.

Study materials were written in English and translated into French, German, Italian, and Spanish. The study protocol and all qualitative materials were submitted to a US independent institutional review board (Pearl IRB, 29 E McCarty St #100, Indianapolis, IN 46225, US) and received exempt status on 25 April 2023. The materials were submitted to a US institutional review board to ensure the study and its' materials met ethical standards, as this research was not eligible for ethics review in France, Germany, Italy, Spain, or the UK. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Qualitative Data Collection

All participants meeting the inclusion criteria and none of the exclusion criteria were required to complete an informed consent form prior to interview and were able to withdraw from the study at any time. Data were collected through in-depth, one-to-one interviews to allow participants to express their personal experience without the judgment or influence of others. The interviews were conducted using online or virtual platforms such as Zoom, Microsoft Teams, or Skype, and lasted 60 minutes for people living with schizophrenia and caregivers, and 45 minutes for prescribers. All interviews were completed in the local language, and were audio recorded and transcribed in English.

This study took a qualitative descriptive approach during interviews to ensure the information gathered aligned with the naturalistic description of patient and caregiver experiences and preferences, with minimal interference from the researcher.³² A qualitative descriptive approach aims to gather a straight description and comprehensive summary on specific questions and allows flexibility to interpret data in a meaningful manner.³² Reliability in applying qualitative description was established by using the concepts of descriptive and interpretive validity.³³

Participants received a country-specific fair market value incentive for their time, in accordance with the Sponsor's compliance regulations. The study was anonymized, with no personal identifying information collected for use in the analysis. A double-blind approach was used, such that the identities of the Sponsor and participants were unknown to each other before and during the interview. Participants in France, Germany, Italy, and Spain were informed of the

Sponsor's name at the end of the interview, in line with General Data Protection Regulations. Participants in the UK were also informed of the Sponsor's name at the end of the interview, in line with the British Healthcare Business Intelligence Association guidance.

Data Analysis

Qualitative data analysis software, MAXQDA, was used to review the verbatim transcripts and code the data. A bottom-up approach to coding was used, relying on inductive coding to develop concepts and themes from the raw data. Coding was completed in layers: to begin, a member of the study team systematically read the text, formed understandings and established a code system driven by topics in the interview guide. A second level of coding further focused on the data, using thematic analysis to identify richer and more detailed findings by themes, driven by the research objectives. Throughout the coding process, the study team reviewed these codes intermittently to establish patterns, identify new concepts and make refinements to ensure central themes were relevant to the study objectives.

Overall data saturation for people living with schizophrenia and caregivers was assessed with the goal of identifying code saturation in core themes.³⁴ Code saturation was not assessed for prescribers as prescriber data were meant to supplement data collected from people living with schizophrenia. The study team remained open to all insights emerging from the data and all concepts were coded. To ensure data quality and limit biases, both data collection and analysis followed the Consolidated Criteria for Reporting Qualitative Research,³⁵ and the Standards for Reporting Qualitative Research.³⁶

Results

Fifteen people living with schizophrenia, 11 caregivers of people living with schizophrenia, and 13 prescribers participated in individual interviews as part of this study. Study participant characteristics from France, Germany, Italy, Spain, and the UK are presented in Table 3 (see [Supplementary Table 1](#) for a breakdown of participant characteristics data by country). By the last interview, no new concepts associated with perceptions of LAIs, treatment preferences, and thoughts on an LAI given every 2 months were identified for people living with schizophrenia and caregivers, indicating that data saturation was achieved.

Table 3 Study Participant Characteristics

	People Living with Schizophrenia (n=15)
Age (years), min, max	29, 59
Gender, n	
Male	13
Female	2
Time since diagnosis (years), n	
0–6	5
7–12	9
13–30	1
Current LAI, n	
1 st generation	3
2 nd generation	12
Time on once-monthly LAI, n	
≥3 months but <6 months	2
≥6 months ^a	13
Receiving concomitant oral medication for schizophrenia, n	
Yes	3
No	8
Not asked/did not provide information	4

(Continued)

Table 3 (Continued).

	People Living with Schizophrenia (n=15)
Level of education, n	
Less than high school/completed some high school	6
High school graduate or equivalent (eg, GED)	1
Completed at least some college or technical school	1
College graduate (eg, BA, BS, AB)	1
Completed at least some graduate school (eg, MS, MD, PhD, PharmD)	5
Unknown	1
	Caregivers (n=11)
Age (years), min, max	43, 74
Gender, n	
Male	1
Female	10
Current LAI received by person they care for living with schizophrenia, n	
1 st generation	4
2 nd generation	3
Not mentioned	4
Time person living with schizophrenia for whom they provide care has been on once-monthly LAI, n	
≥3 months but <6 months	0
≥6 months ^b	11
Person living with schizophrenia for whom they provide care receiving concomitant oral medication for schizophrenia, n	
Yes	6
No	3
Not asked/did not provide information	2
	Prescribers (n=13)
Time in practice (years), min, max	16, 30
Number of schizophrenia patients per month, min, max	12, 80
LAI prescriptions per month, min, max	5, 50
Setting, n	
Private	2
Hospital	5
Hospital and outpatient clinic	3
Private and outpatient clinic	1
Outpatient clinic	1
Hospital, outpatient and prison	1

Notes: ^aDuring interviews, more precise information was obtained about the time the person living with schizophrenia had been treated with a once monthly LAI: ≥6 months but <1 year (n=2), 1–5 years (n=8), and 6–15 years (n=3); ^bduring the interviews, more precise information was obtained about the time the care recipient had been treated with a once monthly LAI: ≥6 months but <1 year (n=1), 1–5 years (n=2), 6–15 years (n=1), ≥16 years (n=3), unknown (n=4).

Abbreviations: AB, Artium Baccalaureus; BA, Bachelor of Arts; BS, Bachelor of Science; GED, general educational development; LAI, long-acting injectable; MD, Doctor of Medicine; MS, Master of Science; PharmD, Doctor of Pharmacy; PhD, Doctor of Philosophy.

People living with schizophrenia included in the study had transitioned from oral medication to an LAI for several reasons. These reasons included lack of compliance, not doing well on their current medication, reaching a crisis point, side effects, the convenience of an LAI, or general interest in an LAI compared with oral medication. People living with schizophrenia reported that they primarily learned about LAIs from their doctor or during hospitalization for an acute phase.

Their doctors described the LAI as “more manageable”, “easier” and that it may result in “less worry”. Some doctors mentioned that the “drug would be the same as the oral therapy”, and that “the LAI had worked for their other patients”.

Healthcare Experiences of People Living with Schizophrenia and Caregivers

People living with schizophrenia and caregivers typically experienced limited barriers to accessing care. They reported living close to a large city or near their doctor’s office and had their cost of care covered through their country’s healthcare system. For those that experienced challenges in finding and receiving care, these included long waiting times, lack of consistent care, limited specialist availability, and time and cost spent attending appointments. Some challenges, such as doctors being dismissive of patient needs or needs not being met, led to negative experiences of seeking care. Experiences of stigma and judgement also led to hesitancy in engaging with healthcare providers, with one caregiver from Italy saying,

This illness is surrounded by stigma... it’s not easy to be understood because the problems we face are different than anyone else’s.

Caregivers described the stress and burden of providing support, which impacted their daily lives and the ability to work. The support role of caregivers included providing help with personal care, cooking, finances, and keeping appointments, in addition to encouraging treatment adherence, independence with daily tasks, and societal engagement. One caregiver from Italy noted,

Before my son’s disease, I liked going to the gym, walking in the park, and riding a bike. I absolutely cannot do it anymore because I must take care of my son.

Caregivers experienced an emotional toll from supporting people living with schizophrenia who lacked insight into their condition or did not accept their diagnosis.

When talking about current treatment (a once-monthly LAI), people living with schizophrenia and caregivers expressed mixed views. Treatment with a once-monthly LAI was described as “easy”, “balanced” and “comfortable”; receiving the injection was viewed as part of their routine, and they valued phone reminders from their doctor ahead of appointments. One person living with schizophrenia from Germany said,

Well, I’m definitely glad that I no longer have to take the tablets every day, because I sometimes forgot to take them. And somehow, I feel a bit liberated from it, although, when the day comes when I have to go there, I don’t really like that either. But it’s better than taking tablets every day and at least I’ll have peace of mind for a month.

Caregivers described a fear that the medication may stop working and several people living with schizophrenia indicated they were “bored” with appointments, with one person from Spain saying,

I see a lot of waiting time... things stop for a bit and when I take the medication once a month it kind of hinders, so to speak, the rest of my responsibilities.

When asked for one thing they would improve about their current once-monthly LAI, people living with schizophrenia would reduce the frequency of administration, while caregivers prioritized a reduction in side effects and less need for oral supplementation.

Shared Decision-Making

When asked about their involvement in treatment decisions, the experiences of people living with schizophrenia varied. They commonly reported being involved in discussions but trusting their physician or caregiver for the final decision, while some worked with their physician to make the final decision. People living with schizophrenia who were not involved in decision-making also experienced having no choice in treatment selection due to the severity of their illness at the time or complying with their doctor. Caregivers responded that they often took part in treatment decision-making but placed trust in the doctor and deferred to their recommendations, or reported leaving the final decision to the person living with schizophrenia. Where caregivers did make the final treatment choice, they did their best to involve the person living with schizophrenia, and where the person was not doing well the caregiver described making the decision to ensure they would get better. Prescribers revealed that several factors affect caregiver involvement in decision-making, such as

the patient's desire for privacy, the relationship between the patient and caregiver, and the patient's age and duration of family support.

Although people living with schizophrenia and caregivers commonly reported having no questions during treatment decisions as they trusted their doctor or viewed them as being “in charge”, they did detail the information that was most important to them when learning about treatment or LAIs specifically (Figure 1).

A common concept captured in the interviews was that people living with schizophrenia and caregivers did not search for information on treatment in general, with some leaving decisions to their doctor or avoiding searching for information as they found it scary or inaccurate. Similarly, they often reported that they did not research LAIs before starting on the treatment, and instead expressed that they had confidence and trust in their doctor.

Prescribers described spending time with patients and caregivers to share information on treatment options, discuss goals, and highlight quality of life benefits. Regarding the behaviors of patients living with schizophrenia and caregivers around treatment selection, prescribers reported that they received questions on efficacy and side effects. Patients also queried whether they needed medication and the effects it might have on their personality, while caregivers questioned whether treatment would improve patients' autonomy, including washing themselves and engaging socially. When moving from an oral to an LAI antipsychotic, patients and caregivers queried prescribers on the differences in side effects, duration of effect, and impact on having a child. Typical concerns shared with prescribers about LAIs specifically related to the amount of medication given at one time, fear of needles and injection site pain, the stigma that receiving an injectable means a more serious and chronic disease, and loss of autonomy or feeling that an LAI is punitive. One psychiatrist from Germany noted,

It's possible that patients may be confused by how LAIs work at a lower dose over a longer period of time, but if I say that, I usually don't tell, I draw it. I draw a curve where the concentration course of a long-term preparation, and on top, I draw the curve of an oral medication, and then patients see very quick which one has more dosage and which less.

While prescribers often described presenting various treatment options to patients and caregivers, some encouraged LAIs specifically due to the benefits they had observed in other patients. Other prescribers reported that they present only one

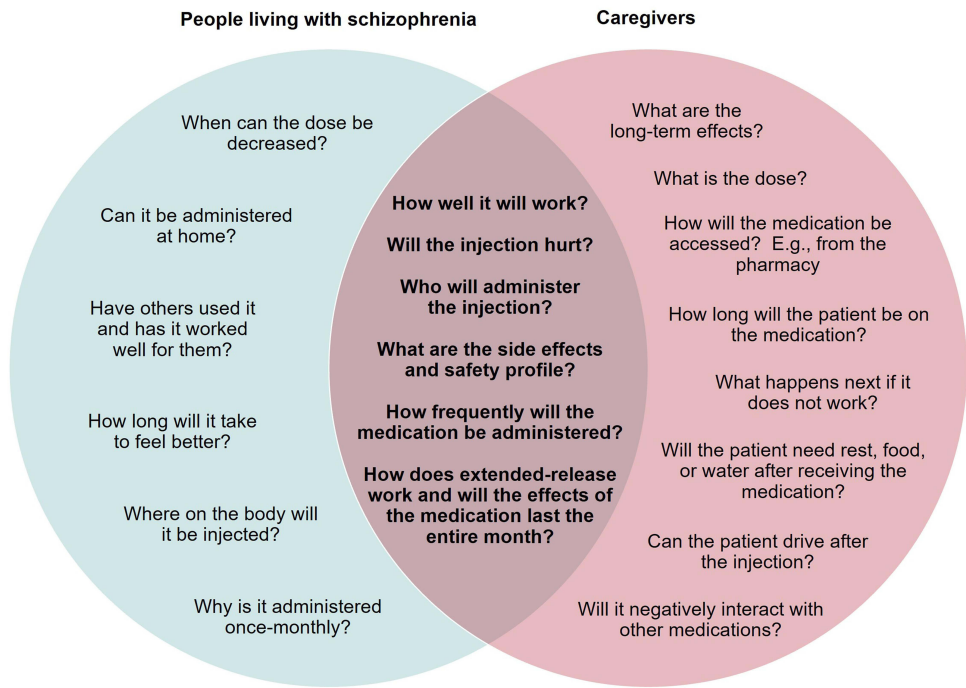


Figure 1 Information viewed as most important by people living with schizophrenia and caregivers when learning about treatment options, specifically LAIs.

treatment option, to increase patient confidence and reduce decision anxiety, while giving further information to allow for an open-ended discussion.

When discussing treatment options, prescribers viewed caregivers as allies, though they typically do not make the final treatment decision. One psychiatrist from the UK mentioned,

I like to involve [the family] as much as they want to be involved and as much as the patient is happy for them to be involved...
It's not just doctors working with patients, but caregivers and friends and family and society...

Prescribers emphasized the importance of patient awareness of their condition and the need for treatment and sought to establish a trusting relationship with their patients to build this understanding. One psychiatrist from Spain shared,

Schizophrenia is a disease that sounds as something severe, it sounds as something 'very hard', both for caregivers but also for patients when they have certain disease awareness. But we must talk about it, we must destroy the myths surrounding it, and then, from that demystification, we must make them understand that it's a chronic disease, and as it is a chronic disease, it requires a chronic treatment.

Treatment Goals

In their responses to questions on treatment goals, participants mentioned the common themes of wishing for the person living with schizophrenia to be clinically stable leading to a reduction in symptoms and emotional outbursts, and for treatment to be effective and result in the patient feeling "balanced" (Figure 2).

Prescribers described their primary treatment goal as improved quality of life, which encompassed the ability to work, be productive, enjoy life, and have functional relationships with family and friends. Stability, in terms of avoiding positive or negative symptoms, was similarly important, and quality of life and stability were often described together, implying that they go hand-in-hand for patients living with schizophrenia.

Perceptions of LAIs for People Living with Schizophrenia and Caregivers

In terms of perceptions of LAIs, people living with schizophrenia and caregivers often viewed remaining on the same medicine and having a choice of where the LAI is injected as the most important features, with other factors playing a lesser role in LAI selection (Table 4).

Reasons Behind the Decision to Prescribe an LAI

Prescribers identified a range of patient, caregiver, physician and medication themes that were important to consider when making the decision to prescribe an LAI (Table 5). They highlighted the important role played by caregivers in keeping the physician informed of how the patient was doing, and in supporting with adherence. Patient buy-in was seen as a critical factor in treatment success, as were dosing frequency and previous treatment response due to prescriber preference for patients remaining on the same molecule when transitioning to an LAI. Prescribers also noted that the use of an LAI provided certainty that patients with advanced, severe, chronic disease had received medication.

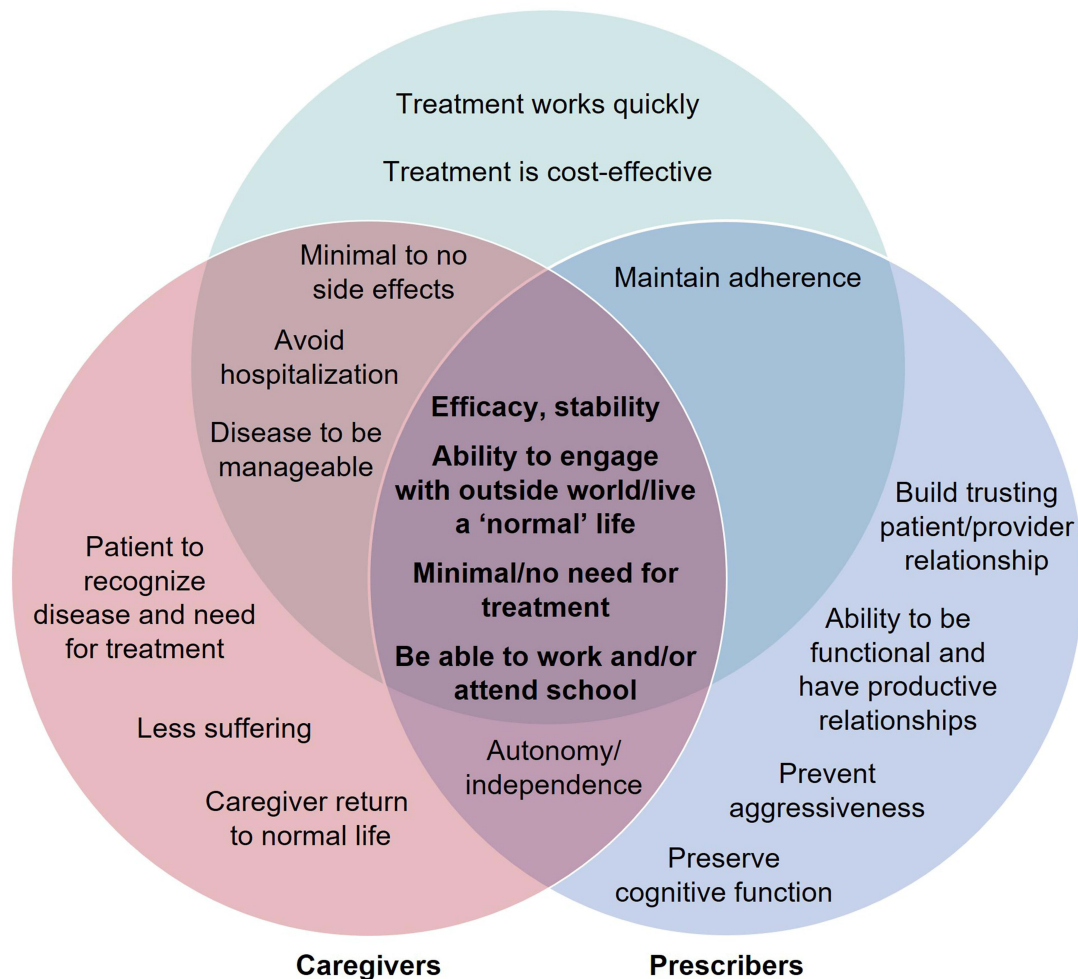
Views on an LAI Administered Every 2 Months

People living with schizophrenia and caregivers generally expressed positive views about an LAI with a 2-month dosing frequency, describing it with words such as "great", "better", "calm", and "free". Participants often highlighted the perception that such a treatment would be convenient and less burdensome than their current treatment (Table 6). They indicated that visiting their psychiatrist once every 2 months would be acceptable, especially if visits aligned with injection appointments and treatment was going well. However, both people living with schizophrenia and caregivers stated that disease stability is prioritized over convenience.

Similarly, prescribers responded that an LAI given every 2 months would be received positively by patients due to convenience, less injection pain, and feeling more normal due to receiving fewer injections (Table 6). When asked about perceived disadvantages, prescribers highlighted a perceived lack of need, loss of dosing "control", less frequent visits with patients experiencing issues, and the potential need for supplemental oral antipsychotics (Table 6).

"I want to achieve such a state that other people consider me very normal or likeable. Sometimes it's a heavy burden on me when I get a flare-up. I want those flare-ups to disappear. And I want to be able to live a very consistent, regular life, much like everybody else."
 Person living with schizophrenia, Germany

People living with schizophrenia



"I want her disease to be manageable and for her to be able to recognize her disease and her need for medication. That the medication stabilizes her and she is able to live her day-to-day life. If that would work, that would be fantastic. That would be like a bar of gold."
 Caregiver, Germany

"The goals are to make sure no dangerous behaviour disorder emerges. Then, it's to make sure that they meet society's requirements as much as possible."
 Psychiatrist, France

Figure 2 Treatment goals among people living with schizophrenia, caregivers and prescribers.

Prescribers stated that they were open to recommending an LAI given once every 2 months to patients stable on an oral medication or the associated once-monthly LAI, or for those expressing a preference for a decreased dosing frequency or for LAIs in general. Other suitable patients included those demonstrating prior adherence to treatment, and those who may benefit due to a busy schedule (eg, with work or school).

Table 4 Perceptions of the Feature of LAIs and on the Features of an “Ideal” Treatment Among People Living With Schizophrenia and Caregivers

Perceptions of the features of LAIs	<p>More frequently mentioned features:</p> <p>Remaining on the same medicine</p> <p>Choice of where on their body to receive the injection</p> <p>Frequency and method of administration (ie, pill or injection)</p> <p>Less frequently mentioned features:</p> <p>Amount of medication in each injection^a</p> <p>Who administers the injection^b</p> <p>Location of administration (eg, doctor's office)</p>	<p>“We must keep the same one [medicine]! We can't change like that!... Switching treatments might not work for me. And trying a medication again when one did work is not conceivable.” Person living with schizophrenia, France</p> <p>“I think he would gladly take one and only one medication, rather than taking half of this, 5 drops of that, and so on.” Caregiver, Italy</p>
Features of an “ideal” treatment	<p>More frequently mentioned features:</p> <p>Efficacious</p> <p>Decreased frequency of administration compared with once-monthly LAI</p> <p>Minimal or no side effects</p> <p>Less frequently mentioned features:</p> <p>An injectable for convenience</p> <p>A pill to avoid injection-site pain</p> <p>Option to administer at home/self-administer</p> <p>Ability to lessen the amount of co-medications</p> <p>More time and freedom</p> <p>Less stress and responsibility in daily life for patients and caregivers</p> <p>Feeling more “normal” and less burdened by their illness</p>	<p>“It would make me safe and I wouldn't have to watch out for any appointments. I could move about more freely even in the long term. ...It would absolutely give me more safety and, as they say, more quality of life.” Person living with schizophrenia, Germany</p> <p>“It would give him a better lifestyle, basically, because he rarely leaves the house. As far as helping me, I just want to see my son getting well, you know?” Caregiver, UK</p>

Notes: ^aAs long as side effects are minimal or absent, participants did not place much importance on amount of medication in each injection; ^bpreferences for a skilled, consistent and personable healthcare practitioner.

Abbreviation: LAI, long-acting injectable.

Discussion

In previous studies that have evaluated LAIs with dosing intervals longer than one month, people living with schizophrenia and caregivers reported the benefits of improved flexibility and convenience,^{29,30} and reduced treatment and caregiver burden.^{25,26,29} A reduced dosing frequency was also reported to be less stigmatizing,^{28,30} reduce the patient's focus on illness,²⁹ increase their involvement in daily activities and social interactions,^{28,29} and may lead to improved quality of life and overall level of adherence.¹⁴ Further benefits were noted by physicians and nurses, who experienced improved communication with their patients.²⁸

The present qualitative, single-person interview study reflects many of these experiences, and builds on these findings by providing insights from people living with schizophrenia, caregivers, and prescribers about a hypothetical LAI given every 2 months rather than a specific treatment. Over the course of the interviews, people living with schizophrenia and caregivers shared a range of perspectives and, by the last interview, no new concepts were identified. This suggests that the sample size was appropriate and that the interviews achieved data saturation, consistent with previous evidence suggesting that it takes 12 interviews to attain saturation.³⁷ All three participant groups reported a general acceptance for an LAI given once every 2 months, perceiving that it would bring greater freedom and a reduced treatment burden. Caregiver burden can reduce quality of life for people living with schizophrenia⁵ and, for some patients and caregivers in this study, less caregiver involvement and burden were factors that may influence acceptance of an LAI given once every 2 months. However, despite the perceived benefits, people living with schizophrenia and caregivers unequivocally prioritized symptom stability over convenience. Overall, these findings indicated that dosing once every 2 months was viewed as a treatment option that would fit in with patients' and caregivers' everyday lives, and aligned with prescribers' preferences for providing holistic care for their patients that encompasses improved efficacy, tolerability, self-agency, and freedom from burden.

Table 5 Prescriber Views of Important Factors for Consideration When Prescribing an LAI

Theme	Details	Prescriber Views
Support	Caregiver or family involvement	Caregivers may be influential in patients starting an LAI Caregivers may play an important role in keeping the physician apprised of the patient's progress Caregivers may assist with adherence
Medical history	Treatment adherence	LAI may alleviate previous challenges with compliance, such as symptom return due to lack of adherence to oral medication
	Previous treatment response	Efficacy and concerns for side effects or allergies influence prescriber preference for patients to remain on the same molecule when transitioning to an LAI
Patient features	Treatment preferences	Desire for autonomy and fear of needles negatively influence LAI acceptance Patient buy-in on treatment is important
	Patient characteristics	Younger patients or those experiencing a first episode may benefit most from LAIs to “get the most out of the patient” LAIs may be preferred for patients with substance abuse issues, who may experience challenges with compliance LAIs may bring flexibility to patients who are working or travelling, allowing them to avoid daily medication May be more likely to prescribe LAIs for men, as women are perceived as more compliant, less likely to be violent, and may be of childbearing age
	Patient symptoms	LAIs may be beneficial in advanced, severe, chronic disease to ensure medication is received LAIs may be required for sedation due to aggression
	Patient residence	May be less likely to prescribe LAIs for patients in assisted living or prison as compliance is “less of an issue” ^a
Dosing schedule	Reduced dosing frequency	May increase compliance May reduce stress around forgetting medication Allows for patient preference to be acknowledged
	Appointment frequency	May want to see patients more frequently than the dosing schedule
Treatment features	Side effects	May lead to patients stopping treatment
	Need for oral supplementation	Some accept oral supplementation may be necessary for the best outcomes Some hope to avoid oral supplementation due to concerns about drug–drug interactions
Logistics	Access to medication	LAIs may be selected to reduce patient burden based on proximity to injection location and accessibility to transportation
Control	Physician dosing control and patient autonomy	Physicians may feel they cannot control medication in cases where dose changes are needed or side effects need to be addressed Patients may feel a loss of autonomy and view treatment as punitive

Note: ^aPrescribers continued to acknowledge the value of LAIs for these patients.

Abbreviation: LAI, long-acting injectable.

During interviews, participants from all groups indicated that a decreased frequency of clinic visits was acceptable provided symptoms remained stable, and a preferable feature of an ideal treatment for people living with schizophrenia and caregivers. Prescriber responses indicated that they saw the value of less frequent dosing in terms of allowing patients to feel normal due to receiving fewer injections and would consider this approach in clinically stable patients and those expressing a wish for reduced dosing. However, it is important that prescribers take the opportunity to consult with their patients outside of injection visits as needed, rather than appointments becoming associated purely with the administration of treatment.

Table 6 Perceptions of the Advantages and Disadvantages of an LAI Administered Every 2 months Versus a Once-Monthly LAI

Participant Group	Perceived Advantages	Perceived Disadvantages
People living with schizophrenia and caregivers	<p>Convenience Less time attending and thinking about appointments</p> <p>Personal impact Similar or improved and sustained efficacy and stability Fewer or no side effects Staying on the same medicine Fewer injections; less responsibility; improved relationships; ability to go on vacation Feeling “free”, “serene” and more “normal”</p> <p>Associated burden Reduced impact on caregivers</p>	<p>Duration of effect Medication not working or being less effective than their current treatment Medication wearing off before next dose Changes may be minimal</p> <p>Organization Difficulty in remembering when an injection is due; forgetting appointments</p> <p>Tolerability Potential for additional side effects Exacerbation of post-injection site pain</p>
Prescribers	<p>Physician benefits Lessening the frequency of visits with stable patients and freeing up time for patients needing more support Decreasing overall workload</p> <p>Patient benefits Fewer appointments and injections, leading to patients experiencing less frequent pain, feeling more normal, less burdened by treatment and having more freedom More treatment options Patient may feel well and be more stable for longer with a gradual release of medication Fewer side effects</p> <p>Overall Patients feeling positive due to fewer visits, fewer injections (and so less pain) and feeling more normal due to less treatment</p>	<p>LAI need May be no need for an extended formulation given the availability of other medication frequencies, with patients doing well on once-monthly LAIs</p> <p>Control Inability to “tweak” or “control” dosing if side effects occur; linking visits to injections may lead to fewer visits with patients who are less stable</p> <p>Efficacy Potential lack of duration of efficacy leading to the need for oral supplementation</p>

Abbreviation: LAI, long-acting injectable.

Perceived disadvantages included the fear that a dosing interval of once every 2 months may mean the effects of the medication would lessen before the next injection, with no option to alter dosing and, therefore, the potential need for supplemental oral antipsychotics. It is noteworthy that, although these are concerns that are applicable to all LAIs,³⁸ the decrease in plasma concentrations of an antipsychotic is much more gradual after the end of the dosing period with an LAI compared with oral dosing.³⁹ Although “wearing off” of medication may be a concern, pharmacokinetic studies of antipsychotic drugs have confirmed the maintenance of stable blood levels throughout the dosing interval with LAIs,^{40,41} which provides the benefits of consistent bioavailability and fewer plasma peaks compared with oral antipsychotics.⁴² For example, evidence shows that efficacious concentrations of medication are maintained for the full dosing interval with the recently approved LAI formulation of aripiprazole monohydrate, which is administered once every 2 months compared to its once-monthly formulation.^{40,43} Furthermore, comparable efficacy has been demonstrated with aripiprazole administered once-monthly and once every 2 months for the maintenance treatment of schizophrenia, with all patients demonstrating clinical stability.⁴⁴ Finally, a meta-analysis of 115 randomized clinical trials highlighted that some LAIs are associated with fewer side effects and better tolerability compared with oral formulations of the same antipsychotic.⁴⁵

The findings of this study have revealed important insights into LAI use in the management of schizophrenia and the experiences of patients. By detailing this study’s results relating to participants’ healthcare experiences, shared decision-making, and treatment goals ahead of those relating to the primary objective, we have sought to provide the context of their general views of disease management and treatment ahead of presenting their perceptions of an LAI given every 2

months. Interview findings highlighted that people living with schizophrenia do not always share their questions and concerns about treatment with their physician. This emphasizes the importance of shared decision-making and the need for prescribers to engage the patient in conversation to establish if they have any preconceptions about LAIs, such as the perceptions that LAIs signify a greater severity of disease or the effects of the medication may lessen before the next injection. Such discussions ensure that prescribers have the opportunity to address concerns or misconceptions preemptively and identify ways to support patients with adherence. However, evidence suggests that shared decision-making is underutilized for people with psychiatric disorders.⁴⁶ Consequently, interventions to promote shared decision-making, such as training for physicians and patients or use of decision aids, may improve use of this approach.⁴⁶

Strengths and Limitations

A strength of this study is its qualitative research design, which allowed participant insights to be examined in depth to enable a full understanding of treatment preferences and the factors influencing these decisions. Study interviews were semi-structured, meaning participants were not restricted to specific questions but could be guided and redirected by moderators in real time as new information emerged. The study also drew from a diverse range of participants, in terms of age and geographical location, and the extensive experience of prescribers in the management of schizophrenia; however, it should be noted that the majority of people living with schizophrenia were male and caregivers were female.

Qualitative research may be associated with researcher and participant bias, which may limit its findings. To minimize this effect, moderators were briefed in the subject matter and received instruction on the use of the discussion guide. For concept elicitation research, data are collected from a relatively small number of individuals and thus findings are not intended to be generalizable to a larger population; the value of qualitative research is the representation of key values and opinions that are important to the populations being studied. These data can then be used to generate hypotheses regarding the study populations and provide direction on further investigation. Additionally, as the insight of people living with schizophrenia was not formally assessed, it was not possible to determine the extent to which schizophrenia may have impaired insight for this participant group, and the impact on their opinions and preferences for treatment. The potential impact of impaired insight was likely reduced by excluding participants with a current acute episode, when insight is usually most impacted.⁴⁷ Although this does not rule out the possibility of impaired insight, understanding the patient perspective was key to the objectives of the study, regardless of level of insight. Finally, although the sample size was small, data saturation was reached for people living with schizophrenia and caregivers and, although this was not assessed for prescribers, results were concordant between all three participant groups. Concordance between the three participant groups further indicates that the views of people living with schizophrenia are unlikely to have been biased by impaired insight.

Conclusion

In this qualitative interview study participants expressed overall positive views on a potential transition to an LAI given once every 2 months. The findings indicate that there may be general acceptance of an LAI administered once every 2 months for the treatment of schizophrenia given the perceived advantages of greater freedom and less treatment burden. Treatment selection of a specific LAI should acknowledge individual patient and caregiver preferences regarding formulation and frequency, to ensure that targeted disease management goals are met. In particular, this study indicates that treatment duration and efficacy are critical factors for uptake.

This qualitative analysis is intended to be hypothesis generating, and the insights gathered will inform the development of a larger, one-time, cross-sectional, quantitative survey to evaluate preferences for an LAI given once every 2 months.

Data Sharing Statement

To submit inquiries related to Otsuka clinical research, or to request access to individual participant data (IPD) associated with any Otsuka clinical trial, please visit <https://clinical-trials.otsuka.com/>. For all approved IPD access requests, Otsuka will share anonymized IPD on a remotely accessible data-sharing platform.

Ethics Approval and Informed Consent

The study protocol and all qualitative materials were submitted to a US independent institutional review board (Pearl IRB, 29 E McCarty St #100, Indianapolis, IN 46225, US) and received exempt status on 25 April 2023. This research was not eligible for ethics review in France, Germany, Italy, Spain, or the UK.

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Author Contributions

All authors made a significant contribution to the work reported, whether that was in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Consent for Publication

Written informed consent for the publication of their anonymized statements was obtained from study participants at the beginning of the study. Participant consent was reiterated verbally prior to the initiation of participant interviews.

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Clodagh Beckham is a full-time employee of Otsuka Pharmaceutical Europe Ltd.

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