

Preferences for Selecting and Initiating Long-Acting Injectable Antipsychotic Agents for the Treatment of Patients With Schizophrenia: Results From the US DECIDE Survey

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Background: Long-acting injectable antipsychotics (LAIs) improve adherence and reduce schizophrenia relapse rates. Data on which LAI attributes drive clinician preference are limited. **Methods:** In the DECIDE survey, 380 psychiatric clinicians (psychiatrists, psychiatric nurse practitioners, and physician assistants) were surveyed regarding preferences when selecting and initiating LAIs for patients with schizophrenia. Responses were analyzed by clinician use of LAIs (high [$\geq 31\%$ of their patients using LAIs] or low [$\leq 14\%$ of their patients using LAIs]) and mindset toward LAI use (early, severity reserved, adherence reserved, and LAI hesitant). **Results:** Overall and across subgroups, side effects were the most important consideration when selecting a particular LAI, with 33% of clinicians ranking this as most important (26%–46% across subgroups). Clinician preference for the molecule was most often ranked least important (47% overall; 39%–59% across subgroups). A significantly higher proportion of clinicians with high vs low LAI use ranked product attributes as the most important consideration (26% vs 13%; $P < .01$). Across subgroups, multiple injection site options, small/on par needle, and price made at least two-thirds of clinicians somewhat/much more likely to use a particular LAI, and 63%–82% of clinicians reported being somewhat/much more likely to select an LAI dosed once monthly or less often vs 6%–11% being somewhat/much more likely to select an LAI dosed once every 2 weeks. **Conclusions:** Overall, results from DECIDE provide insight into the decision-making process of

psychiatric clinicians when selecting an LAI and highlight opportunities to help clinicians deliver optimal care for patients with schizophrenia.

Key words: adherence; barriers; mindset; side effects; dosing.

Introduction

In addition to controlling symptoms, preventing relapse is a key goal of antipsychotic (AP) treatment for schizophrenia.¹ Importantly, relapses have broad implications, such as disruption in social, educational, and work settings, increased risks of hospitalization and violence toward self and others, financial costs, and resistance to further treatment because of slower onset of response and reduced efficacy.¹ The most frequent cause of relapse is poor adherence to oral antipsychotic (OA) medications.²

Compared with OAs, long-acting injectable antipsychotic (LAI) medications are associated with greater adherence,^{3–9} as well as lower rates of relapse/hospitalization,^{7–17} mortality/suicidal behavior,^{16–18} and inpatient/emergency department visits.^{6–8} Despite their benefits, clinicians tend to reserve LAIs for patients with more severe symptoms or adherence issues^{19–22}; yet, expert opinion suggests that LAIs could be used earlier in the disease course and before adherence issues arise.^{1,23–26} Other barriers to LAI use reported by clinicians include

perceived patient fear/dislike of needles, expectation of patient refusal, costs, perception that current OA therapy is adequate, lack of knowledge regarding the use of LAIs, concerns about the specifics of LAIs (eg, injection frequency, injection site requirements), and side effects.^{20,21,25,27,28} Although barriers to the use of LAIs have been described, limited information is available on why some clinicians are more able/willing to prescribe LAIs and use them for a broader set of clinical situations, as well as which characteristics of LAI formulations clinicians prefer.

The DETERmining Clinician Factors for Implementing LAIs and DEFeating Barriers (DECIDE) study was designed to assess knowledge, experience, attitudes, and barriers to LAI use among psychiatric clinicians treating patients with schizophrenia in the United States (US). The primary analysis of DECIDE showed that clinicians often underestimated rates of nonadherence and that many were not confident using LAIs.²⁹ Similar to other studies,^{19–21} many clinicians reserved LAIs for patients with adherence issues (68%) or more severe disease (37%). DECIDE was also designed to compare subgroups of psychiatric clinicians based on their self-reported level of LAI use among patients with schizophrenia or their self-reported mindset related to LAI use. Practice environment, attitudes, motivation, and confidence varied between clinicians from different subgroups, particularly between those with a mindset of using LAIs as early as possible vs those who were hesitant to use LAIs; however, across subgroups, similar proportions of clinicians agreed that most patients taking OAs will eventually relapse or have adherence issues and that LAIs are a good early treatment option for patients with schizophrenia. The objective of the present analysis of the DECIDE study was to describe the criteria clinicians used for selecting LAIs, as well as preferences for LAI characteristics, both in the overall study population and in subgroups of clinicians reporting high or low LAI use and those with differing mindsets toward the use of LAIs.

Methods

Survey Design and Execution

A survey was developed to assess US-practicing clinicians' knowledge, experience, attitudes, and barriers related to the use of LAIs for patients with schizophrenia, as described previously.²⁹ The survey was developed in collaboration with a clinical expert and pilot-tested with 4 practicing clinicians from the target audience. The final version included 44 questions and was estimated to take approximately 15 min to complete. The survey consisted of multiple choice and Likert-based questions, as well as questions prompting clinicians to estimate prescribing practices (eg, proportion of patients with schizophrenia taking an LAI) and practice characteristics (eg, race, insurance coverage status of their patients

with schizophrenia). Questions focused only on the use of APs in patients with schizophrenia. The sponsor, Teva Branded Pharmaceutical Products R&D, Inc., reviewed and approved the survey, and the Western Institutional Review Board (Puyallup, WA, USA) exempted the research project from institutional review board oversight under the Common Rule 45 CFR section 46.104(d)(2) (research only included interactions involving survey procedures, and there were adequate provisions to maintain participant privacy and confidentiality).

The survey was distributed to US-based psychiatrists, psychiatric nurse practitioners (NPs), and psychiatric physician associates (PAs) by CE Outcomes via direct email to a national database of clinicians (from Northeastern, Midwestern, Southern, and Western regions of the US) who have previously participated in similar research and to clinician contacts obtained through purchase of vendor lists. Respondents provided informed consent before completing the survey and, upon survey completion, respondents were provided a \$50 USD incentive. Survey responses were collected using an online survey platform. Partial responses were not accepted by the system, and respondents were prompted to answer unanswered questions. Responses were considered valid if the survey was fully completed.

Potential respondents were screened using questions that asked about role, specialty, and number of patients with schizophrenia. Additional screening questions asked about self-reported view of LAIs ("mindset") and the percentages of patients with schizophrenia taking APs that they managed with oral vs LAI formulations. Eligible clinicians indicated psychiatry as their specialty and managed ≥ 1 patient with schizophrenia per month. Recruitment goals were also set for clinician type (physician and NPs/PAs; goal of approximately 295 physicians and 85 NPs/PAs) and mindset (goal of equal enrollment across mindsets); once these quotas were met, additional potential respondents within those categories were screened out.

Analysis Populations

In prespecified analyses, responses were summarized for the full study population and in clinician subgroups defined by LAI use and LAI mindset. The prespecified analysis also included an evaluation of response in subgroups based on clinician role (physician and NP/PA), practice setting (community and academic), and practice location (urban, suburban, and rural). LAI use and LAI mindset are not entirely independent of one another; however, for the purposes of this article, they were considered as different models for grouping LAI prescribers in order to detect trends in LAI preferences.

For the LAI-use subgroup analyses, clinicians were categorized based on their response to the screening question in which they estimated the proportion of

patients with schizophrenia in their practice taking APs who were using LAIs. Among the responses provided, 3 subgroups were defined by percentiles: low (1st-33rd percentile; $\leq 14\%$ of patients taking APs using LAIs), mid (34th-67th percentile; 15%-30% using LAIs), and high (68th-100th percentile; $\geq 31\%$ using LAIs). Only clinicians categorized into the high and low LAI-use subgroups were included in analyses of these data; the mid LAI-use subgroup was not analyzed to increase chances of detecting clinically significant differences.

For the LAI mindset subgroup analyses, the mindset was identified using the survey question, "Which of the following best fits the current way you view your use of [LAIs] for your patients with schizophrenia?" Clinicians who selected the response "I actively use LAIs as early as possible for my patients" were categorized into the early-use mindset. The severity-reserved mindset consisted of clinicians selecting the response "LAIs are reserved for patients with more severe symptoms, or later in the patient journey when other treatments have failed." The adherence-reserved mindset included clinicians who selected the response "LAIs are reserved for patients with identified adherence issues to oral medication." The LAI-hesitant mindset included clinicians who expressed hesitation to use LAIs, based on the response "I'm hesitant to recommend LAIs due to a concern or barrier (lack of experience, access, etc.) but would consider using them more" or "LAIs do not offer a significant advantage vs OAs for my patients or are worth 'the work'."

Statistics

Based on power calculations using the number of known clinicians in this specialty in the US and the aim to have a margin of error under $\pm 5\%$, a total of 380 respondents were sought. Altogether, 1168 clinicians were invited to participate. Data were summarized using descriptive statistics. Chi-square and *t*-tests comparing the clinician subgroups were conducted on all items of the survey using Qualtrics (Provo, UT) and SPSS 27 (IBM: Armonk, NY). No adjustments were made for multiplicity testing.

Results

Respondent and Practice Characteristics

As described previously,²⁹ the survey was distributed between March and July of 2022 to 1168 clinicians. Valid survey responses were received from 380 psychiatric clinicians (295 psychiatrists, 74 psychiatric NPs, and 11 psychiatric PAs), most of whom were in a community-based practice (82%) and urban (44%) or suburban (42%) locations. Based on the range of values reported by the clinicians, high and low LAI-use categories were defined as use in $\geq 31\%$ and $\leq 14\%$ of patients, respectively. According to these cutoffs, 106 (28%) clinicians were categorized as having high LAI use and 130 (34%)

were categorized as having low use. When categorized by mindset, the early-use mindset subgroup included 123 (32%) clinicians, the severity-reserved mindset included 88 (23%), the adherence-reserved mindset included 113 (30%), and the LAI-hesitant mindset included 56 (15%). Clinicians in the early-use mindset subgroup were more likely to report LAI use that was categorized as high LAI use ([Supplementary Table S1](#)).

Responder demographics have been described previously.²⁹ Clinicians reported an average of 20 years in psychiatry practice (SD, 11). Clinicians with high LAI use saw more patients with schizophrenia each month (mean 88 patients [SD, 159]) than those with low use (27 [34]; $P < .01$). In addition, clinicians with low LAI use reported that significantly more patients were on commercial or private medical insurance compared with clinicians who reported high LAI use (35% vs 25%, $P < .05$). Significantly fewer patients of low LAI users used Medicaid insurance (29% vs 41%, $P < .01$) compared with high LAI users; respondent demographics and practice characteristics were otherwise similar between the 2 LAI-use subgroups. Clinicians with an early-use mindset saw more patients with schizophrenia each month (mean 99 patients [SD, 168]) than those from the other mindset subgroups ($P < .01$; 50 [45], 38 [41], and 18 [21] in the severity-reserved, adherence-reserved, and LAI-hesitant subgroups, respectively; $P < .01$ for LAI-hesitant vs severity- and adherence-reserved). Clinicians with an early-use mindset also had a greater proportion of patients taking LAIs (mean 42% [SD, 20] vs 22% [16], 19% [16], and 8% [15], respectively; $P < .01$ for early-use vs other mindsets; $P < .01$ for LAI-hesitant vs other mindsets), as well as patients on Medicaid insurance (43%, $P < .01$ vs severity-reserved), compared with other mindsets. Clinicians with a severity-reserved mindset reported that most of their patients were on commercial or private (31%, $P < .05$ vs early-use) and Medicare insurance (32%, $P < .05$ vs adherence-reserved), with clinicians with adherence-reserved mindset reporting the highest proportion of uninsured patients (12%, $P < .05$ vs severity-reserved) vs other mindsets. Clinicians reported having means of 8 [SD, 12], 7 [12], 4 [4], and 5 [11] support staff individuals (nurses or medical assistants) in the early-use, severity-reserved, adherence-reserved, and LAI-hesitant mindset subgroups, respectively ($P < .01$ for early-use vs adherence-reserved; $P < .05$ for severity-reserved vs adherence-reserved).

Criteria for LAI Selection

Respondents were asked to rank 5 criteria that they might consider when selecting their LAI of choice from most important to least important ([Table 1](#)). The criteria included side effects and what the patient will tolerate, preference for the molecule, access (pricing, whether LAI is included in the formulary, and sample availability),

Table 1. Most Important and Least Important Criteria for the Selection of an LAI

Ranking, <i>n</i> (%)	Overall (<i>n</i> = 380)	LAI use subgroups		LAI mindset subgroups			
		High LAI use (<i>n</i> = 106)	Low LAI use (<i>n</i> = 130)	Early use (<i>n</i> = 123)	Severity re- served (<i>n</i> = 88)	Adherence re- served (<i>n</i> = 113)	LAI hesi- tant (<i>n</i> = 56)
Side effects and what the patient will tolerate							
1 = most important	126 (33)	28 (26)	47 (36)	34 (28) [§]	25 (28) [§]	41 (36)	26 (46)
2	123 (32)	37 (35)	38 (29)	40 (33) [§]	35 (40) ^{§§}	39 (35) [§]	9 (16)
3	83 (22)	24 (23)	25 (19)	27 (22)	20 (23)	21 (19)	15 (27)
4	37 (10)	12 (11)	17 (13)	16 (13)	6 (7)	10 (9)	5 (9)
5 = least important	10 (3)	5 (5)	2 (2)	6 (5)	2 (2)	2 (2)	0 (0)
Preference for molecule							
1 = most important	80 (21)	24 (23)	25 (19)	31 (25) ^{§§}	23 (26) ^{§§}	22 (19) [§]	4 (7)
2	23 (6)	6 (6)	9 (7)	7 (6)	6 (7)	6 (5)	4 (7)
3	31 (8)	9 (8)	12 (9)	10 (8)	7 (8)	8 (7)	6 (11)
4	65 (17)	20 (19)	24 (18)	27 (22) [‡]	17 (19)	13 (12)	8 (14)
5 = least important	180 (47)	47 (44)	59 (45)	48 (39) ^{†‡§}	35 (40) ^{‡§}	64 (57)	33 (59)
Access (pricing, on formulary, readily available samples, etc.)							
1 = most important	76 (20)	21 (20)	32 (25)	26 (21)	16 (18)	19 (17)	15 (27)
2	85 (22)	21 (20)	26 (20)	28 (23)	19 (22)	26 (23)	12 (21)
3	66 (17)	23 (22)	22 (17)	16 (13)	19 (22)	22 (19)	9 (16)
4	81 (21)	24 (23)	24 (18)	25 (20)	18 (20)	27 (24)	11 (20)
5 = least important	71 (19)	17 (16)	25 (19)	28 (23)	16 (18)	19 (17)	8 (14)
Preference for product attributes							
1 = most important	72 (19)	28 (26) ^{**}	17 (13)	25 (20)	21 (24) [§]	21 (19)	5 (9)
2	69 (18)	17 (16)	24 (18)	19 (15)	18 (20)	21 (19)	11 (20)
3	100 (26)	26 (25)	35 (27)	38 (31)	22 (25)	28 (25)	12 (21)
4	96 (25)	22 (21)	38 (29)	28 (23) [§]	19 (22) [§]	28 (25)	21 (38)
5 = least important	42 (11)	13 (12)	15 (12)	13 (11)	8 (9)	15 (13)	6 (11)
Patient preference							
1 = most important	61 (16)	21 (20)	17 (13)	22 (18)	18 (20) [‡]	11 (10)	10 (18)
2	72 (19)	21 (20)	29 (22)	25 (20)	10 (11)	21 (19)	16 (29) ^{††}
3	97 (26)	21 (20)	37 (28)	29 (24)	19 (22)	32 (28)	17 (30)
4	83 (22)	21 (20)	23 (18)	20 (16) [‡]	21 (24)	34 (30)	8 (14) [‡]
5 = least important	65 (17)	21 (20)	23 (18)	26 (21) [§]	20 (23) [§]	15 (13)	4 (7)

Bold font denotes significant values.

**P* < .05,

***P* < .01 vs low LAI use;

†*P* < .05,

††*P* < .01 vs severity-reserved mindset;

‡*P* < .05,

‡‡*P* < .01 vs adherence-reserved mindset;

§*P* < .05,

§§*P* < .01 vs LAI-hesitant mindset.

^aIncluding considerations related to pricing, whether the LAI is on formulary, or has readily available samples.

^bIncluding attributes such as dosing interval and whether multiple body sites can be used as the site of injection. LAI, long-acting injectable antipsychotic.

preferences for product attributes (dosing and injection site), and patient preference (for one LAI over another). Side effects were ranked as the most important consideration by the largest proportion of respondents

(33% overall). Although preference for the molecule was ranked as the least important consideration by the largest proportion of respondents overall (47%), 21% of clinicians (the second highest proportion of clinicians)

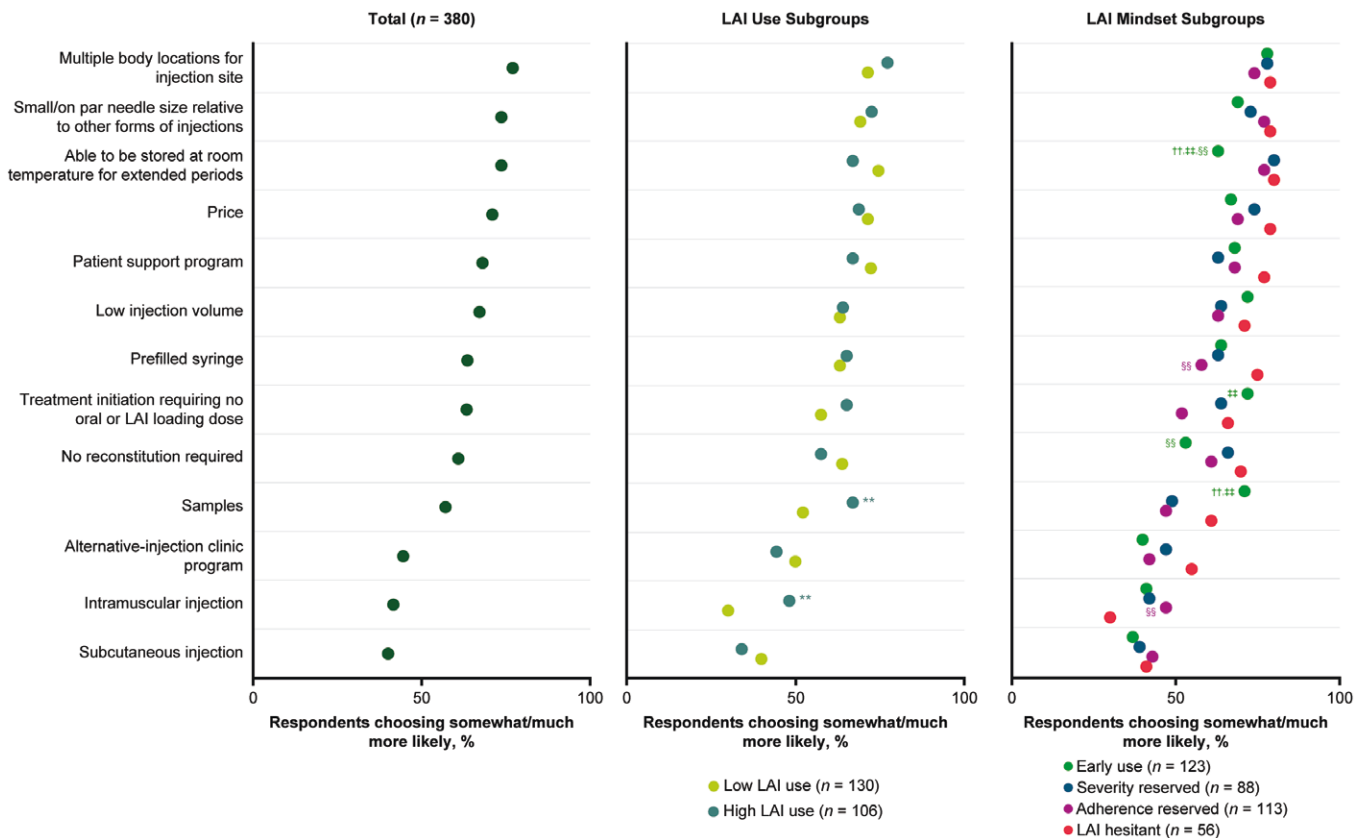


Figure 1. Characteristics Influencing LAI Selection. * $P < .05$, ** $P < .01$ vs Low LAI Use; † $P < .05$, †† $P < .01$ vs Severity-Reserved Mindset; ‡ $P < .05$, ‡‡ $P < .01$ vs Adherence-Reserved Mindset; § $P < .05$, §§ $P < .01$ vs LAI-Hesitant Mindset. LAI, Long-Acting Injectable Antipsychotic.

ranked preference for the molecule as the most important consideration.

Considering the LAI-use subgroups, clinicians with high LAI use most often ranked side effects (26%) and preference for product attributes (26%) as the most important considerations. A similar proportion of clinicians with low LAI use considered side effects to be the most important consideration (36%); however, a smaller proportion rated preference for product attributes as most important compared with the high use subgroup (13%; $P < .01$).

Among mindset subgroups, side effects were ranked as the most important consideration by the highest proportion of respondents in all subgroups. This proportion was highest for clinicians in the LAI-hesitant mindset subgroup (46%) compared with the other mindset subgroups (28%-36%), with significant differences compared with the early-use ($P < .05$) and severity-reserved ($P < .05$) mindset subgroups. Preference for the molecule was ranked as least important by the largest proportion of clinicians across mindset subgroups. In addition, significantly higher proportions of clinicians with LAI-hesitant (59%) or adherence-reserved (57%) mindsets considered this the least important consideration compared with early-use (39%) and severity-reserved (40%) mindsets

($P < .05$ for LAI-hesitant or adherence-reserved vs the other mindset subgroups).

Results among the subgroups based on clinician role, practice setting, and practice location were generally similar to the overall findings and across subgroups (Supplementary Table S2). A higher proportion of psychiatrists reported preference for the molecule as the most important consideration compared with psychiatric NPs/PAs (24% vs 12%; $P < .05$), and a lower proportion of psychiatrists reported this criterion as least important (43% vs 62%; $P < .01$). In addition, a higher proportion of psychiatric NPs/PAs ranked patient preference as most important (25% vs 14% [psychiatrists]; $P < .05$), while a higher proportion of psychiatrists ranked this criterion as least important (19% vs 9% [psychiatric NPs/PAs]; $P < .01$).

Preferred LAI Characteristics

Respondents were asked to rate how certain characteristics and features would influence their choice to use a particular LAI on a 5-point scale from “much less likely to use” to “much more likely to use.” Overall and across subgroups, having multiple injection site options, small/on par needle, and price made at least two-thirds of

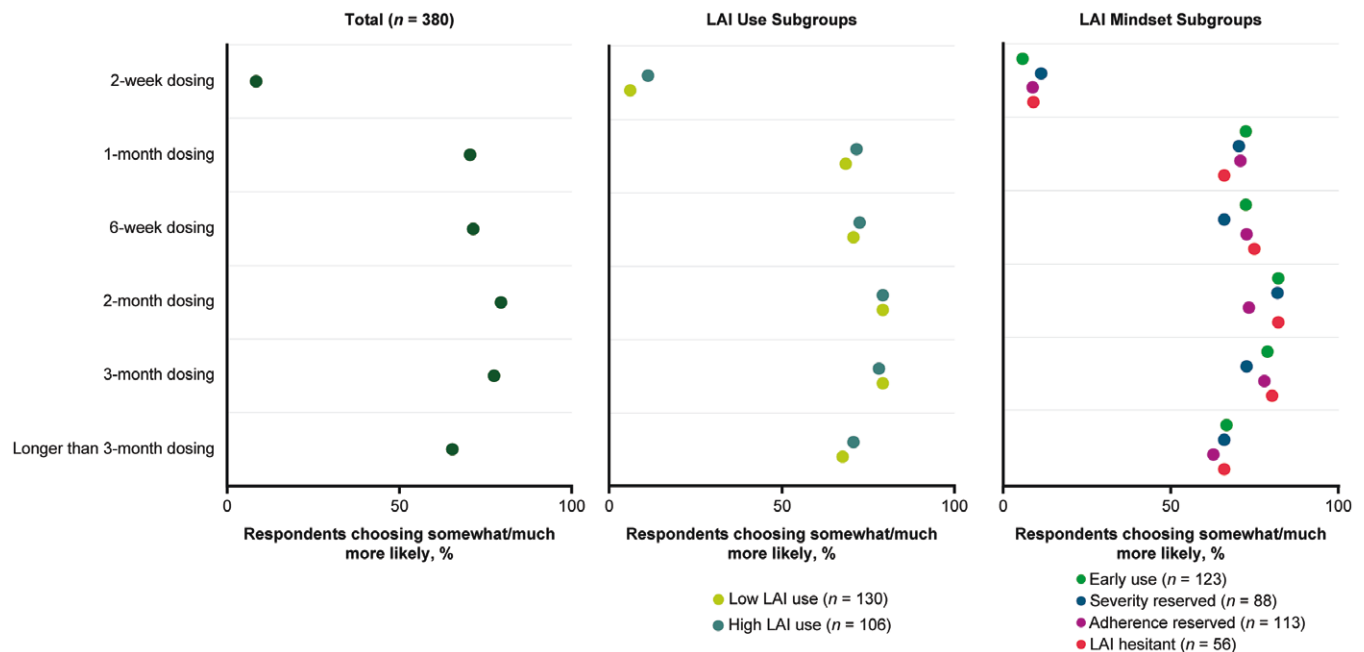


Figure 2. Dosing Intervals Influencing LAI Selection. LAI, Long-Acting Injectable Antipsychotic.

clinicians “somewhat more likely” or “much more likely” to use a particular LAI (Figure 1 and Supplementary Figure S1). In the LAI-use subgroups, ratings were similar for most characteristics; however, a greater proportion of clinicians in the high LAI-use subgroup were “somewhat” or “much more” likely to choose a particular LAI based on samples being available (67% vs 52% for low use; $P < .01$) or based on a requirement for an intramuscular injection (48% vs 35%; $P < .01$).

Responses between LAI mindset subgroups were also largely similar (Figure 1); however, variations were noted. A lower proportion of clinicians from the early-use mindset subgroup reported being “somewhat” or “much more” likely to choose a particular LAI based on being able to store the product at room temperature (63% vs 77%-80%; $P < .01$ compared with other mindset subgroups) or based on the lack of a requirement for reconstitution (53% vs 61%-70%; $P < .01$ for comparison with LAI hesitant). A higher proportion of clinicians from the early-use mindset subgroup reported being “somewhat” or “much more” likely to choose a particular LAI based on samples being available (71% vs 47%-61%; $P < .01$ for comparisons with severity-reserved and adherence-reserved mindsets). Higher proportions of clinicians from the LAI-hesitant mindset subgroup reported that the availability of a prefilled syringe (75% vs 58%-64% for other mindset subgroups; $P < .01$ vs adherence-reserved) led them to be “somewhat” or “much more” likely to choose a particular LAI.

Psychiatrists and psychiatric NPs/PAs had generally similar responses. Clinicians from community and academic practices also had generally similar responses, although a lower proportion of community-based

clinicians reported subcutaneous injection as a feature leading to more likely selection of a particular LAI (37% vs 51%; $P < .01$). Among clinicians with different practice locations, sample availability was the only characteristic with observable differences between subgroups: a higher proportion of clinicians in rural practices (72%) noted this as leading them to be “somewhat” or “much more” likely to select a particular LAI compared with clinicians in urban locations (52%; $P < .01$).

An additional question asked respondents to rate the importance of different dosing intervals on their decision to choose a particular LAI, with responses provided on a 5-point scale from “much less” to “much more” likely to use (Figure 2 and Supplementary Figure S2). At least 65% of clinicians reported being “somewhat” or “much more” likely to select an LAI dosed once monthly or less frequently, and 74% of clinicians indicated that they would be “much less” or “somewhat less” likely to choose an LAI if it required dosing once every 2 weeks. These responses were consistent across LAI-use and mindset subgroups: more than 60% of clinicians across subgroups were “somewhat” or “much more” likely to select an LAI dosed once monthly or less frequently and more than 65% would be “much less” or “somewhat less” likely to select an LAI with dosing once every 2 weeks.

Discussion

The DECIDE study is, to our knowledge, the most comprehensive study to date examining attitudes and preferences among psychiatric clinicians around the use of LAIs in patients with schizophrenia. This included investigating preferences regarding criteria for selecting

an LAI among clinicians with different reported levels of LAI use and different mindsets. Across the clinicians surveyed, results showed that the side-effect profile was the most important consideration when selecting an LAI. However, clinicians from the high LAI-use subgroup were more likely to prioritize product attributes compared with those with low LAI use. Among the mindset subgroups, clinicians in the LAI-hesitant mindset subgroup were more likely to prioritize patient preference when selecting an LAI while deprioritizing product attributes compared with the other mindset subgroups.

Clinicians rated product characteristics that simplify administration (having multiple injection sites, small/on par needle size, and less frequent dosing) as meaningful considerations when choosing an LAI. The availability of samples was selected by those in the high LAI-use and early-use mindset subgroups as an LAI characteristic that would lead them to be somewhat or more likely to choose an LAI. This was more noted by clinicians in rural regions compared with urban or suburban regions, as well as in community centers compared with academic settings. This is possibly due to systemic factors, such as limited resources, transportation difficulties, and other logistic issues which limit the prescription of LAI to patients.³⁰ This study could not investigate social determinants of health in detail, but future studies will investigate this further. In addition, fewer clinicians in the early-use mindset subgroup indicated that room temperature storage or a requirement for reconstitution were attributes that would make them somewhat or more likely to choose an LAI compared with the other mindset subgroups, suggesting these clinicians did not see such attributes (or lack thereof) to be barriers to using LAIs. Across subgroups, more than 60% of clinicians reported a preference for dosing once monthly or less frequently. While fewer clinicians ranked intramuscular injection and subcutaneous injection as characteristics somewhat or much more likely to influence their choice of an LAI, features related to the injection, such as smaller needle and low injection volume, were considered more important. This suggests that future development of LAIs should take into consideration formulations that are less frequently administered, with a smaller needle and injection volume giving patients a choice of injection site.

Consistent with a previous survey study in which 408 frequent LAI prescribers (≥ 1 patient/month with schizophrenia treated with LAIs) were recruited from a nationwide panel from the US in 2020 and completed an online survey,¹⁹ product price was also a notable consideration in treatment decision-making in DECIDE. Patient and caregiver involvement in the treatment decision has been reported as an important part of deciding to start LAIs,¹⁹ though results from DECIDE indicate that when identifying which LAIs to use, patient preference generally is not a key consideration. Although this may

indicate that patients do not express preferences for particular LAIs or that clinicians do not prioritize patient perspectives on which LAI is prescribed, further research is needed to explore this. This could be a key priority for further education on the therapeutic alliance between clinician and patient. The earlier survey study also found that prescriber experience in managing adverse events related to LAIs was an important consideration for frequent LAI prescribers.¹⁹ Results from the previously published analysis of DECIDE support the idea that clinicians who used LAIs more frequently were more likely to be familiar with the associated adverse events.²⁹ In the earlier analysis, clinicians in the high LAI-use and early-use mindset subgroups reported significantly higher levels of confidence in managing side effects than those in the corresponding other subgroups ($P < .01$).²⁹ Furthermore, clinicians in the severity- and adherence-reserved mindset subgroups reported significantly higher levels of confidence in managing side effects than clinicians from the LAI-hesitant mindset subgroup ($P < .05$).²⁹

Results from DECIDE showed that choice of injection location, flexibility in the dosing schedule, and small needle size were important attributes of LAIs. Moreover, 64% and 61% of clinicians indicated that a prefilled syringe and reconstitution, respectively, would make them somewhat or much more likely to select a particular LAI.

In terms of limitations, data from the DECIDE survey were derived from a select sample of US-based clinicians who agreed to participate in an email-based survey. Whether these data are generalizable to other clinicians in the US or other regions is unknown. Data resulting from this and other surveys of this type reflect subjective opinions and are, therefore, inexact and susceptible to recall bias. Furthermore, survey responses were considered valid only if all questions were answered but estimates such as the proportion of patients treated with an LAI were not validated against data from the clinician's practice. In addition, data were limited to the questions asked, and follow-up to clarify responses was not possible. It is possible that a respondent may have misinterpreted a question. In the analysis, no adjustments were made for multiplicity testing. In addition, patient preferences, family input, training issues, stigma, reasons for preference of a specific molecule, and many other aspects driving selection for certain LAIs were not further explored in this study. The use of quotas to ensure responses from clinicians with different training or different subgroups of interest (eg, mindsets) also limited the generalizability of the results. There were also limitations on time and the length of survey, and therefore questions were structured to investigate as many variables as possible which can then be further explored in future studies.

The DECIDE study surveyed clinicians on their preferences for LAIs, but in order to improve rates of LAI use, it is important to also understand which

aspects of LAIs are preferred by patients. The recently completed Attitudes DriVing regional differences in long-acting injectable antipsychotic utilization for schizophrenia among healthcare professionals, patients, and Caregivers (ADVANCE) study questioned clinicians, patients, and caregivers about preferred LAI characteristics and will expand on the results from DECIDE to elucidate similarities and differences between stakeholder preferences.^{31,32}

In conclusion, these results provide insight into psychiatric clinicians' decision-making regarding LAI selection, including among subgroups of clinicians with different levels of LAI use and different mindsets related to the use of LAIs. The side-effect profile was rated as the most important consideration when selecting an LAI, regardless of subgroup. Furthermore, having multiple injection site options, small/on par needle, and price were rated as important product attributes both overall and across subgroups, which could inform future LAI development strategies. These findings highlight opportunities to help clinicians deliver optimal care to their patients with schizophrenia.

Supplementary Material

Supplementary material is available at Schizophrenia Bulletin Open online.

Acknowledgments

The medical writing support was provided by Meredith Kalish, MD, CMPP, and Jennifer C. Jaworski, MS, BCMAS, CMPP, and editorial support by Kelsey Gribbon, MS, all of Ashfield MedComms, an Inizio company, and was funded by Teva Branded Pharmaceutical Products R&D, Inc.

Funding

This work was supported by Teva Branded Pharmaceutical Products R&D, Inc.

Conflicts of Interest

Dawn Velligan has received medical writing support from CE Outcomes; consulting fees from Alkermes, Boehringer Ingelheim, Indivior, Janssen, and Otsuka; travel support from Alkermes and Otsuka; and advisory board support from Merck, Janssen, and Otsuka. Gregory D. Salinas and Emily Belcher are employees of CE Outcomes, LLC, which has received payments from Teva Pharmaceuticals in relation to this study. Kelli R. Franzenburg, Mark Suett, Stephen Thompson, and Rolf T. Hansen III are employees and shareholders of Teva Pharmaceuticals.

References

1. Kane JM, Correll CU. Optimizing treatment choices to improve adherence and outcomes in schizophrenia. *J Clin Psychiatry*. 2019;80:1N18031AH–1N18031C.
2. Kaplan G, Casoy J, Zummo J. Impact of long-acting injectable antipsychotics on medication adherence and clinical, functional, and economic outcomes of schizophrenia. *Patient Prefer Adherence*. 2013;7:1171–1180.
3. Duncan EJ, Woolson SL, Hamer RM. Treatment compliance in veterans administration schizophrenia spectrum patients treated with risperidone long-acting injectable. *Int Clin Psychopharmacol*. 2012;27:283–290.
4. Mahlich J, Olbrich K, Wilk A, Wimmer A, Wolff-Menzler C. Time to treatment discontinuation in German patients with schizophrenia: long-acting injectables versus oral antipsychotics. *Clin Drug Investig*. 2021;41:99–113.
5. Schwartz S, Lee S, Coble EB, Troxler C, Toscano S, Kumar A. Time-to-therapy discontinuation in patients newly diagnosed with schizophrenia initiated on long-acting injectable versus oral dopamine receptor blocking agents. *Early Interv Psychiatry*. 2023;17:921–928.
6. Shah A, Xie L, Kariburyo F, Zhang Q, Gore M. Treatment patterns, healthcare resource utilization and costs among schizophrenia patients treated with long-acting injectable versus oral antipsychotics. *Adv Ther*. 2018;35:1994–2014.
7. Patel C, Emond B, Lafeuille MH, et al. Real-world analysis of switching patients with schizophrenia from oral risperidone or oral paliperidone to once-monthly paliperidone palmitate. *Drugs Real World Outcomes*. 2020;7:19–29.
8. Zhdanova M, Lin D, Lafeuille MH, et al. Antipsychotic adherence, resource use, and costs before and after the initiation of once-monthly paliperidone palmitate therapy among Medicaid beneficiaries with prior schizophrenia relapse. *Clin Ther*. 2021;43:535–548.
9. Dickson MC, Nguyen MM, Patel C, et al. Adherence, persistence, readmissions, and costs in Medicaid members with schizophrenia or schizoaffective disorder initiating paliperidone palmitate versus switching oral antipsychotics: a real-world retrospective investigation. *Adv Ther*. 2023;40:349–366.
10. Tiihonen J, Mittendorfer-Rutz E, Majak M, et al. Real-world effectiveness of antipsychotic treatments in a nationwide cohort of 29 823 patients with schizophrenia. *JAMA Psychiatry*. 2017;74:686–693.
11. Kim HO, Seo GH, Lee BC. Real-world effectiveness of long-acting injections for reducing recurrent hospitalizations in patients with schizophrenia. *Ann Gen Psychiatry*. 2020;19:1.
12. Kishimoto T, Hagi K, Kurokawa S, Kane JM, Correll CU. Long-acting injectable versus oral antipsychotics for the maintenance treatment of schizophrenia: a systematic review and comparative meta-analysis of randomised, cohort, and pre-post studies. *Lancet Psychiatry*. 2021;8:387–404.
13. Gutiérrez-Rojas L, Sánchez-Alonso S, García Dorado M, López Rengel PM. Impact of 3-monthly long-acting injectable paliperidone palmitate in schizophrenia: a retrospective, real-world analysis of population-based health records in Spain. *CNS Drugs*. 2022;36:517–527.
14. Montemagni C, Del Favero E, Cocuzza E, Vischia F, Rocca P. Effect of long-acting injectable antipsychotics on hospitalizations and global functioning in schizophrenia: a naturalistic mirror-image study. *Ther Adv Psychopharmacol*. 2022;12:20451253221122526.

15. Tidmore LM, Keast SL, Waters HC, Pareja KL, Cothran T, Skrepnek GH. Readmissions, costs, and duration to subsequent outpatient visit after hospital discharge among Medicaid beneficiaries utilizing oral versus long-acting injectable antipsychotics in bipolar disorder or schizophrenia. *Curr Med Res Opin.* 2022;38:1621–1630.
16. Fang SC, Huang CY, Shao YJ. Long-term outcomes of early use of long-acting injectable antipsychotics in schizophrenia. *J Clin Psychiatry.* 2022;83:21r–14153.
17. García-Carmona JA, Simal-Aguado J, Campos-Navarro MP, Valdivia-Muñoz F, Galindo-Tovar A. Evaluation of long-acting injectable antipsychotics with the corresponding oral formulation in a cohort of patients with schizophrenia: a real-world study in Spain. *Int Clin Psychopharmacol.* 2021;36:18–24.
18. Huang CY, Fang SC, Shao YJ. Comparison of long-acting injectable antipsychotics with oral antipsychotics and suicide and all-cause mortality in patients with newly diagnosed schizophrenia. *JAMA Netw Open.* 2021;4:e218810.
19. Zhdanova M, Starr HL, Lefebvre P, et al. Understanding the health system conditions affecting the use of long-acting injectable antipsychotics in the treatment of schizophrenia in clinical practice: a US healthcare provider survey. *Neuropsychiatr Dis Treat.* 2022;18:1479–1493.
20. Keenan A, Lin D, Shepherd J, Bailey H, Benson C, 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.
21. Citrome L, Belcher E, Stacy S, Suett M, Mychaskiw M, Salinas GD. Management of schizophrenia with long-acting injectable antipsychotic medications: an assessment of the educational needs of clinicians. *Neuropsychiatr Dis Treat.* 2022;18:111–123.
22. Pilon D, Joshi K, Tandon N, et al. Treatment patterns in Medicaid patients with schizophrenia initiated on a first- or second-generation long-acting injectable versus oral antipsychotic. *Patient Prefer Adherence.* 2017;11:619–629.
23. Sajatovic M, Ross R, Legacy SN, et al. Identifying patients and clinical scenarios for use of long-acting injectable antipsychotics—expert consensus survey part 1. *Neuropsychiatr Dis Treat.* 2018;14:1463–1474.
24. Keepers GA, Fochtmann LJ, Anzia JM, et al.; (Systematic Review). The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia. *Am J Psychiatry.* 2020;177:868–872.
25. Arango C, Fagiolini A, Gorwood P, et al. Delphi panel to obtain clinical consensus about using long-acting injectable antipsychotics to treat first-episode and early-phase schizophrenia: treatment goals and approaches to functional recovery. *BMC Psychiatry.* 2023;23:453.
26. Correll CU, Citrome L, Haddad PM, et al. The use of long-acting injectable antipsychotics in schizophrenia: evaluating the evidence. *J Clin Psychiatry.* 2016;77:1–24.
27. Patel MX, Bent-Enakhil N, Sapin C, et al. Attitudes of European physicians towards the use of long-acting injectable antipsychotics. *BMC Psychiatry.* 2020;20:123.
28. Blackwood C, Sanga P, Nuamah I, et al. Patients' preference for long-acting injectable versus oral antipsychotics in schizophrenia: results from the patient-reported medication preference questionnaire. *Patient Prefer Adher.* 2020;14:1093–1102.
29. Velligan D, Salinas GD, Belcher E, et al. Clinician differences in attitudes and perceptions on the use of long-acting injectable antipsychotic agents in treating patients with schizophrenia: results from the US DECIDE Survey. *BMC Psychiatry.* 2025; in press.
30. Chang HH, Vaughn LM, Liu D. Rural ambulatory care pharmacists providing in-clinic and home visit services improve adherence to long-acting injectable antipsychotics. *Ment Health Clin.* 2024;14:229–232.
31. Franzenburg KR, III HR, Suett M, et al. *Patient and Caregiver Perspectives on Using Long-Acting Injectable Antipsychotics to Treat Schizophrenia: Survey Results From the Multinational ADVANCE Study.* Presented at the 37th European College of Neuropsychopharmacology Congress; September 21–24, 2024; Milan, Italy.
32. Franzenburg KR, III HR, Suett M, et al. *Experiences and Perceptions of Healthcare Professionals With Long-Acting Injectable Antipsychotic Use in Schizophrenia: Survey Results From the Multinational ADVANCE Study.* Presented at the 37th European College of Neuropsychopharmacology Congress; September 21–24, 2024; Milan, Italy.