Physician Characteristics Associated With Prescription of Long-Acting Injectable Antipsychotics

To the Editor: In a comprehensive and elegant review on long-acting injectable antipsychotics (LAIs) published in a recent supplement to the *Journal*, Correll et al reported that "education about the potential benefits of LAIs should be provided to clinicians and the health care team."[1(p17)] My colleagues and I agree with the authors that LAIs have been shown to reduce relapse compared to oral antipsychotics, but their prescribing patterns are not well known.

A recent study conducted in Canada by my colleagues and I investigated prescribing determinants of LAIs among physicians treating schizophrenia using the Quebec drug plan (Régie de l'assurance maladie du Québec [RAMQ]) database. The RAMQ database also includes information on the insured person, such as age, gender, and region, and information on the physicians, such as the period of graduation. Patients with schizophrenia who were incident users of an LAI between January 2008 and March 2012 were selected. Schizophrenia diagnoses were considered confirmed if the last diagnosis related to psychiatric diseases (*ICD-9* codes 290.0–311.9) recorded in the database was one of schizophrenia (*ICD-9* code 295.x).

In this study, 8,230 patients received at least 1 prescription for an LAI. Of these patients, 4,974 did not receive a prescription for an LAI in the year preceding index date (incident users). A total of 3,957 of them were covered by the RAMQ drug insurance for at least 1 year before and 1 year after index date. Finally, 1,996 patients were selected as patients with schizophrenia using an LAI. The general population consisted of a random sample of patients (N = 117,621) enrolled in the RAMQ database. Physician characteristics related to the prescription of the first LAI in the schizophrenia population and prescribing in the general population were compared using the χ^2 test and with a base index of 100, where > 100 indicates an overrepresentation and < 100 indicates an underrepresentation in users with schizophrenia.

Prescribers of LAIs for schizophrenia were more likely to graduate in 1990–1999 (index = 153, $P > .001$) compared to 1970–1979 (index = 63, $P < .001$), more likely to practice in Montréal-Centre than in other areas of Quebec (index = 147, $P > .001$), and more likely to work in both inpatient and outpatient settings (index = 338 and index = 391, respectively, $P > .001$) compared to prescribers for the general population. Data also showed that the use of atypical LAIs compared to typical LAIs was significantly higher ($P < .001$) among younger prescribers (graduation = 1990), in contrast with a significantly higher ($P < .001$) use of typical LAIs among older prescribers (graduation = 1979). The degree of prescribing LAIs appeared to be heterogeneous across the province of Quebec.

In summary, LAI use was more common among recently graduated physicians and those in urban areas and working in both inpatient and outpatient settings.

Reference

1. 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(suppl 3):1–24.

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Cost Reductions Associated With Long-Acting Injectable Antipsychotics According to Patient Age

To the Editor: In their interesting and didactic article, Correll et al state, "The cost of LAIs [long-acting injectable antipsychotics] presents a barrier to their use. However…they may save money across the entire continuum of care."[1(19)] Like other Canadian provinces, Quebec has a universal health care program that covers physician services and hospitalizations for the entire population (Régie de l'assurance maladie du Québec [RAMQ]). This universal health program is complemented, for a large proportion of the population, by a public drug plan. The provincial drug reimbursement program covers all people 65 years and older, beneficiaries of the social assistance program (including individuals with schizophrenia), and individuals who do not have access to a private medication insurance plan. The RAMQ medical services database contains information from physicians' claims for services provided within and outside the hospital. The RAMQ pharmaceutical services database includes information from pharmacists' claims for dispensed medication reimbursed by the program but not for medication received in a hospital. In addition, the program includes an encrypted patient identifier, which enables linkage of individual patient information while preserving anonymity.

A previous study from Quebec, Canada, evaluated the impact of switching to LAIs on health services use in the treatment of schizophrenia.[2,3] More recently, again using the Quebec drug plan database, my colleagues and I selected patients with schizophrenia who were incident users of LAIs between January 2008 and March 2012. The objective was to evaluate the impact of these medications on health care resource utilization (HCRU) in different age groups of patients with schizophrenia. HCRU and associated costs were analyzed during the year before and after LAI initiation, using 5 age groups: < 30, 30–39, 40–49, 50–59, and ≥ 60 years.

The study included 1,996 schizophrenia patients, and their mean age was 43.4 years (SD = 14.5). The mean reductions in hospitalization days and total HCRU costs from the year before to the year after initiation of LAI treatment were 35.1 days (95% CI, 32.0–38.2) and CAD $33,477 (95% CI, 30,347–36,607), respectively (Table 1). Similar reductions in hospitalization days and total HCRU costs were observed across all age groups. In the pre-initiation period, the mean costs associated with the total HCRU were higher among patients younger than 30 years (CAD $69,915) compared to those aged 30 years and over (CAD $54,529) ($P \leq .01$).

This analysis revealed that initiation of LAI treatment was associated with a significant reduction in HCRU in all age groups. Further, in the year before initiation of LAI treatment, costs were higher in younger patients than in older patients.

References

1. 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(suppl 3):1–24.
2. Lachaine J, Lapierre ME, Abdalla N, et al. Impact of switching to long-acting injectable antipsychotics on health services use in the treatment of schizophrenia. *Can J Psychiatry*. 2015;60(suppl 2):S40–S47.
3. Lachaine J, Larbi M, Melnyk P, et al. Impact of initiation of long-acting injectable antipsychotics on resource utilization in patients with schizophrenia. *Value Health*. 2016;19(7):A605.

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Table 1. Age Group and Total Health Care Cost Before and After Introduction of Long-Acting Injectable Antipsychotics

Age Group Comparison (Age Group$_1$ vs Age Group$_2$, y)	n_1	Total Health Care Cost per Patient for Age Group$_1$, Mean (CAD $): Year Preceding Index Date[a]	Total Health Care Cost per Patient for Age Group$_1$, Mean (CAD $): Year Following Index Date	n_2	Total Health Care Cost per Patient for Age Group$_2$, Mean (CAD $): Year Preceding Index Date	Total Health Care Cost per Patient for Age Group$_2$, Mean (CAD $): Year Following Index Date	*P* Value[b]	*P* Value[c]
< 20 vs ≥ 20	21	46,063	32,040	1,975	57,914	24,231	.21	.45
< 25 vs ≥ 25	191	64,263	32,830	1,805	57,105	23,412	.13	.01
< 30 vs ≥ 30	423	69,915	31,888	1,573	54,529	22,276	.00	.00
< 35 vs ≥ 35	673	65,179	29,853	1,323	54,031	21,494	.00	.00
< 40 vs ≥ 40	860	64,041	28,406	1,136	53,057	21,214	.00	.00

[a]The index date was defined as the date of the first prescription for a long-acting injectable antipsychotic between January 1, 2008, and March 31, 2012.
[b]*P* value from independent *t* test of the comparison of mean health care cost in the year preceding index date by age groups.
[c]*P* value from independent *t* test of the comparison of mean health care cost in the year following index date by age groups.

Dr Correll and Colleagues Reply

To the Editor: We thank Dr Stip for his 2 letters[1,2] that were stimulated by our recent report on the characteristics, extant data, and implications pertaining to long-acting injectable antipsychotics (LAIs) in the management of patients with schizophrenia.[3] Drawing on the Canadian Quebec universal health care program that covers physician services and hospitalizations for the entire Quebec population, Dr Stip adds interesting information to the discussion about the potential value of LAIs that is relevant to 2 questions: (1) Which physicians may require additional education about LAI use, as they differentially prescribe LAIs less often? and (2) Is the cost barrier of LAI medications possibly offset by potential health care cost savings associated with LAIs?

Analyzing data from January 2008–March 2012 including 1,996 patients with schizophrenia treated with LAIs under real-world conditions, Dr Stip first investigated characteristics of LAI prescribers.[1] Consistent with prior data, such as from New York State,[4] the degree of LAI prescribing was heterogeneous across the province of Quebec. Moreover, LAI prescribing was less common among physicians who graduated earlier, practiced outside of urban centers, and did not work in both inpatient and outpatient settings.[1]

This type of analysis can be useful to better understand practice patterns and help focus quality improvement efforts. However, prior studies, such as one from Germany,[5] reported results contrary to Dr Stip's analysis. Heres et al found that older psychiatrists, who may be more familiar with LAI use predating the widespread use of oral second-generation antipsychotics, were more likely to prescribe LAIs.[5] Regarding the results provided by Dr Stip, it remains unclear whether prescriber age serves as a proxy for clinical characteristics of caseload. Assuming an average age of 25 years at medical school graduation, these cohorts would have been 45–55 years and 65–75 years of age during the study midpoint of 2010. Thus, the lower LAI prescribing in the older prescriber cohort could be due to a smaller caseload or treating fewer more severely ill patients with schizophrenia. The finding that prescribers working in both inpatient and outpatient settings prescribe more LAIs may point to the fact that prescribers who follow patients across treatment settings are more aware of the frequency and consequences of antipsychotic nonadherence and therefore utilize more LAIs to better bridge the potentially problematic gap between inpatient and outpatient care.

Second, health care costs in the year following LAI initiation were associated with significant health care cost savings compared to the prior year. The cost savings to the province of Quebec was related to lower inpatient care utilization.[2] Although health care costs were higher in the year before initiation of LAIs in younger compared to older patients, cost savings were apparent across all 5 age groups spanning < 20 to ≥ 60 years of age[2]; this underscores our tenet that LAIs should be offered to patients at all illness stages.

Various study designs have investigated the relative effectiveness of oral antipsychotics and LAIs, including mirror-image designs such as that reported by Dr Stip, cohort studies, and randomized controlled trials (RCTs). Each design has pros and cons.[6] Nevertheless, database studies[7] and recent RCTs[8,9] indicate that LAIs have an advantage regarding treatment continuation and relapse/hospitalization over oral antipsychotics in patients early in the course of schizophrenia. These data should be taken into consideration when revising treatment guidelines for schizophrenia, as patients at all stages of the illness could potentially benefit from being offered LAIs. Furthermore, LAIs may also have a role in patients who currently appear treatment adherent, as the risk for nonadherence is high.[10]

References

1. Stip E. Physician characteristics associated with prescription of long-acting injectable antipsychotics. *J Clin Psychiatry*. 2017;78(8):e1060.
2. Stip E. Cost reductions associated with long-acting injectable antipsychotics according to patient age. *J Clin Psychiatry*. 2017;78(8):e1061.
3. 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(suppl 3):1–24.
4. Citrome L, Levine J, Allingham B. Utilization of depot neuroleptic medication in psychiatric inpatients. *Psychopharmacol Bull*. 1996;32(3):321–326.
5. Heres S, Hamann J, Kissling W, et al. Attitudes of psychiatrists toward antipsychotic depot medication. *J Clin Psychiatry*. 2006;67(12):1948–1953.
6. Haddad PM, Kishimoto T, Correll CU, et al. Ambiguous findings concerning potential advantages of depot antipsychotics: in search of clinical relevance. *Curr Opin Psychiatry*. 2015;28(3):216–221.
7. Tiihonen J, Haukka J, Taylor M, et al. A nationwide cohort study of oral and depot antipsychotics after first hospitalization for schizophrenia. *Am J Psychiatry*. 2011;168(6):603–609.
8. Schreiner A, Aadamsoo K, Altamura AC, et al. Paliperidone palmitate versus oral antipsychotics in recently diagnosed schizophrenia. *Schizophr Res*. 2015;169(1–3):393–399.
9. Subotnik KL, Casaus LR, Ventura J, et al. Long-acting injectable risperidone for relapse prevention and control of breakthrough symptoms after a recent first episode of schizophrenia: a randomized clinical trial. *JAMA Psychiatry*. 2015;72(8):822–829.
10. Kane JM, Kishimoto T, Correll CU. Non-adherence to medication in patients with psychotic disorders: epidemiology, contributing factors and management strategies. *World Psychiatry*. 2013;12(3):216–226.

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