Schizophrenia-Related Hospitalization History Before Long-Acting Injectable Antipsychotic Initiation and Its Association With Subsequent Adherence and Hospitalizations Among Dual-Eligibles: The CRITICAL PERIOD Study

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Introduction

- Schizophrenia (SCZ) is a chronic, severe psychiatric disorder associated with substantial clinical, humanistic, and economic burden[1]
- Suboptimal adherence to oral antipsychotics (APs) is common and is a major contributor to relapses, emergency department visits, and SCZ-related hospitalizations[2–4]
- Real-world evidence has demonstrated that long-acting injectable antipsychotics (LAIs) are associated with improved medication adherence and a reduced risk of SCZ-related hospitalizations compared with oral APs[5,6]
- It is theorized that the timing of first LAI use may play a critical role in influencing patient outcomes[7]

Objective

- The CRITICAL PERIOD study intended to examine the SCZ-related hospitalization history prior to initiating an LAI and its association with AP adherence and healthcare resource use in dual-eligible Medicare beneficiaries with SCZ in the United States

Methods

Data source

- Data were taken from 2006 to 2021 national Medicare and Medicaid fee-for-service (FFS) claims available from the Centers for Medicare and Medicaid Services

Sample selection

- All beneficiaries having ≥1 claim with International Classification of Diseases (ICD)-9 code or ICD-10 code of SCZ in any position from the Medicaid or Medicare FFS claims, with the first observed claims occurring between 7/1/2009 and 12/31/2021 (N = 1,338,215)
- Dually eligible for Medicare and Medicaid when they were first eligible for Medicare (n = 340,524)
- ≥1 antipsychotic fill between July 1, 2009, and December 31, 2021, with the first AP fill date occurring on or after the date of the first observed SCZ diagnosis date in Medicare or Medicaid claims (n = 86,110)
- Continuous full Medicaid (fee for service [FFS] or health maintenance organization [HMO]) coverage or Medicare FFS Part D coverage from first SCZ diagnosis date till first AP fill date (i.e. index date) (n = 40,412)
- First eligible for Medicare due to disability (excluding patients aging into Medicare since they likely had private insurance prior to turning 65 years old) (n = 33,102)
- Use of an LAI between July 1, 2009, and December 31, 2021; the first date of LAI use was the index date (n = 11,735)
- Time between the first observed SCZ diagnosis date and first LAI use date (index date) was 1 month or more (n = 10,808)
- Continuous coverage of at least 12 months in the post-index period (to allow a 12-month fixed follow-up period to measure outcomes) (n = 9472)

Independent variable

- Patients were stratified by the number of SCZ-related hospitalizations in the pre-index period (0, 1, 2-5, or ≥6 hospitalizations)

Outcomes

- Adherence to any LAI during the 12-month post-index period
- Adherence to any APs during the 12-month post-index period
- All-cause, any relapse,, mental health–related, and SCZ-related hospitaliations during the 12-month post-index period

Analysis

- Descriptive analyses were conducted on patient characteristics and outcomes in the overall sample and by independent variable
- Logistic regressions were used to assess how the number of SCZ-related hospitalizations during the pre-index period was associated with outcomes, while controlling for demographic and clinical characteristics

Results

- Patients had a median age of 29 years and were primarily male (70%) and non-White (59%, **Table 1**)
  - Over half (54%) of patients had no SCZ-related hospitalizations in the pre-index period; the remaining patients had 1 (21%), 2 to 5 (20%), and ≥6 (4%) SCZ-related hospitalizations, respectively
  - The median time from first observed SCZ diagnosis to first observed LAI initiation was 9 months (5 for 0, 12 for 1, 24 for 2 to 5, and 45 for ≥6 SCZ-related hospitalizations)
- The most frequently used LAIs were paliperidone (44%), haloperidol (19%), and aripiprazole (16%, **Table 2**)

Table 1: Patient characteristics

	Overall (n = 9472)	Number of schizophrenia-related hospitalizations during the pre-index period			
		0 (n = 5154)	1 (n = 2027)	2 to 5 (n = 1893)	≥6 (n = 398)
Age on index date					
Mean (SD)	32.4 (10.2)	32.4 (10.3)	32.3 (10.3)	32.5 (10.1)	32.9 (9.0)
Median (IQR)	29.0 (25.0, 37.0)	29.0 (25.0, 37.0)	29.0 (25.0, 37.0)	29.0 (25.0, 37.0)	30.0 (26.0, 37.0)
Male	6601 (69.7%)	3686 (71.5%)	1365 (67.3%)	1280 (67.6%)	270 (67.8%)
Race					
White	3877 (40.9%)	2025 (39.3%)	872 (43.0%)	808 (42.7%)	172 (43.2%)
Black	2914 (30.8%)	1496 (29.0%)	629 (31.0%)	640 (33.8%)	149 (37.4%)
Hispanic	849 (9.0%)	537 (10.4%)	141 (7.0%)	138 (7.3%)	33 (8.3%)
Other	1461 (15.4%)	877 (17.0%)	302 (14.9%)	243 (12.8%)	39 (9.8%)
Metropolitan status					
Urban	7823 (82.6%)	4247 (82.4%)	1642 (81.0%)	1574 (83.1%)	360 (90.5%)
Days from first observed schizophrenia diagnosis date to index date					
Mean (SD)	569.8 (703.2)	356.6 (544.0)	604.2 (688.8)	920.4 (767.3)	1487.2 (838.5)
Median (IQR)	281.0 (67.0, 816.0)	135.0 (30.0, 423.0)	347.0 (98.0, 857.0)	705.0 (318.0, 1312.0)	1343.5 (768.0, 2018.0)
Without relapses in 1-month pre-index period	6927 (73.1%)	4299 (83.4%)	1366 (67.4%)	1074 (56.7%)	188 (47.2%)
OAP agents used in pre-index period					
Any OAP use	6527 (68.9%)	2811 (54.5%)	1578 (77.8%)	1748 (92.3%)	390 (98.0%)
Haloperidol	1698 (17.9%)	514 (10.0%)	414 (20.4%)	579 (30.6%)	191 (48.0%)
Quetiapine	1809 (19.1%)	668 (13.0%)	386 (19.0%)	558 (29.5%)	197 (49.5%)
Olanzapine	2094 (22.1%)	748 (14.5%)	450 (22.2%)	679 (35.9%)	217 (54.5%)
Risperidone	2967 (31.3%)	1096 (21.3%)	708 (34.9%)	904 (47.8%)	259 (65.1%)
Fluphenazine	421 (4.4%)	124 (2.4%)	95 (4.7%)	150 (7.9%)	52 (13.1%)
Aripiprazole	1893 (20.0%)	798 (15.5%)	417 (20.6%)	508 (26.8%)	170 (42.7%)
Clozapine	400 (4.2%)	136 (2.6%)	79 (3.9%)	124 (6.6%)	61 (15.3%)
Ziprasidone	745 (7.9%)	251 (4.9%)	154 (7.6%)	248 (13.1%)	92 (23.1%)
Paliperidone	906 (9.6%)	357 (6.9%)	208 (10.3%)	269 (14.2%)	72 (18.1%)
Lurasidone	750 (7.9%)	266 (5.2%)	156 (7.7%)	244 (12.9%)	84 (21.1%)
Any other agent	85 (0.9%)	51 (1.0%)	21 (1.0%)	n≥11	n<11
Evidence of mental health–related hospitalization in 30-day pre-index period	1690 (17.8%)	160 (3.1%)	564 (27.8%)	763 (40.3%)	203 (51.0%)

IQR, interquartile range; OAP, oral antipsychotic.

Table 2: Agent of first observed LAI use

	Overall (n = 9472)	Number of schizophrenia-related hospitalizations during the pre-index period			
		0 (n = 5154)	1 (n = 2027)	2 to 5 (n = 1893)	≥6 (n = 398)
FGA LAI					
Fluphenazine	496 (5.2%)	264 (5.1%)	103 (5.1%)	107 (5.7%)	22 (5.5%)
Haloperidol	1765 (18.6%)	865 (16.8%)	407 (20.1%)	403 (21.3%)	90 (22.6%)
SGA LAI					
Aripiprazole	1524 (16.1%)	868 (16.8%)	315 (15.5%)	283 (14.9%)	58 (14.6%)
Olanzapine	135 (1.4%)	65 (1.3%)	28 (1.4%)	28 (1.5%)	14 (3.5%)
Paliperidone	4159 (43.9%)	2289 (44.4%)	894 (44.1%)	810 (42.8%)	166 (41.7%)
Risperidone	1393 (14.7%)	803 (15.6%)	280 (13.8%)	252 (13.8%)	48 (12.1%)

FGA, first generation antipsychotic; LAI, long-acting injectable; SGA, second generation antipsychotic.

- In descriptive analyses, an increasing number of SCZ-related hospitalizations in the pre-index period was associated with lower rates of adherence to any LAI (41% to 23%) and higher rates of any all-cause (26% to 72%), mental health–related (22% to 71%), and SCZ-related (18% to 66%) hospitalization during the 12-month post-index period (**Table 3**)

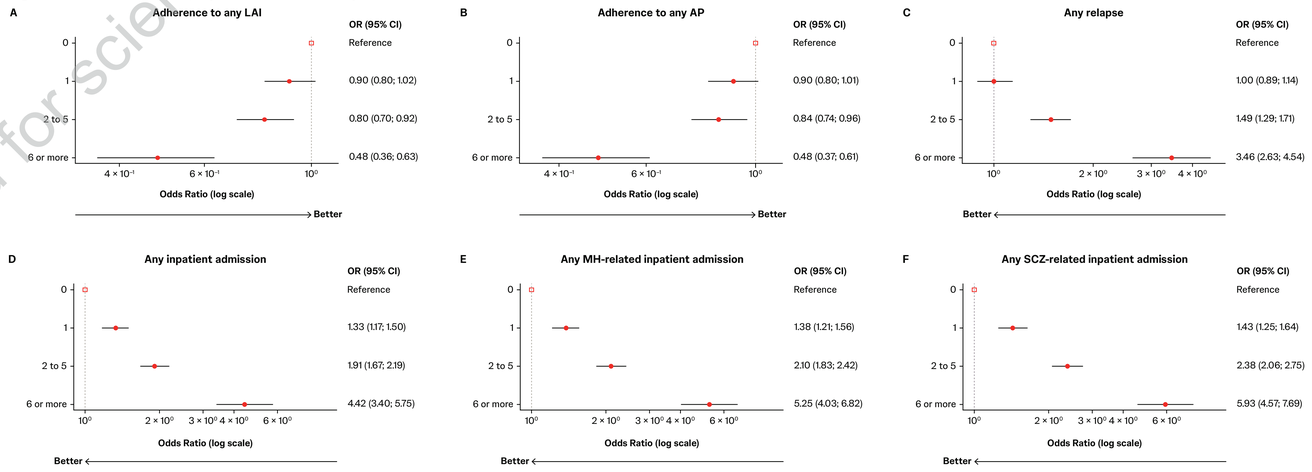
Table 3: Descriptive outcomes

	Overall (n = 9472)	Number of schizophrenia-related hospitalizations during the pre-index period			
		0 (n = 5154)	1 (n = 2027)	2 to 5 (n = 1893)	≥6 (n = 398)
Adherence (PDC≥0.80)					
To any LAI	3571 (37.7%)	2104 (40.8%)	737 (36.4%)	639 (33.8%)	91 (22.9%)
To any antipsychotics	5573 (58.8%)	3116 (60.5%)	1159 (57.2%)	1098 (58.0%)	200 (50.3%)
Hospitalization					
Any inpatient admission	3257 (34.4%)	1320 (25.6%)	740 (36.5%)	912 (48.2%)	285 (71.6%)
Any relapse	4383 (46.3%)	2217 (43.0%)	872 (43.0%)	1008 (53.2%)	286 (71.9%)
Any mental health-related inpatient admission	2939 (31.0%)	1131 (21.9%)	666 (32.9%)	861 (45.5%)	281 (70.6%)
Any schizophrenia-related inpatient admission	2516 (26.6%)	918 (17.8%)	556 (27.4%)	779 (41.2%)	263 (66.1%)

LAI, long-acting injectable; PDC, proportion of days covered.

- Logistic regressions confirmed these results (**Figure 1**)
  - For instance, compared with patients with no SCZ-related hospitalizations, those with 2 to 5 SCZ-related hospitalizations in the pre-index period had lower odds of adherence to any LAI (odds ratio [OR]: 0.80, $P < 0.01$) and higher odds of any all-cause (OR: 1.91, $P < 0.01$), mental health–related (OR: 2.10, $P < 0.01$), and SCZ-related hospitalization (OR: 2.38, $P < 0.01$) in the post-index period
- Sensitivity analyses among patients aged ≤35 years and ≤25 years on index date showed similar findings (data not shown)

Figure 1: Association between prior SCZ-related hospitalizations and outcomes



AP, antipsychotic; LAI, long-acting injectable; MH, mental health; SCZ, schizophrenia.
Y-axis label is the number of SCZ-related hospitalizations during the pre-index period.

Key Takeaways

- Use prior SCZ-related hospitalization count as a practical flag for instability when true onset is uncertain in claims/records; higher pre-index hospitalizations predict poorer adherence and higher relapses post-LAI
- Screen early-phase patients (≤25 at first diagnosis) for LAI candidacy after the first hospitalization rather than waiting for multiple admissions; earlier initiation aligns with lower downstream relapse and hospitalization risk
- For payers and policy actions: Create an "early-LAI" coverage pathway for dual-eligibles newly diagnosed or after first hospitalization (e.g., reduced prior authorization requirements, coverage for in-hospital initiation and post-discharge administration)

Conclusions

- Dual-eligible Medicare beneficiaries with ≥1 SCZ-related hospitalization prior to LAI initiation had lower odds of maintaining AP adherence and higher risk of subsequent SCZ-related hospitalizations
- These findings underscore the importance of timely LAI initiation, as waiting until patients experience one or more SCZ-related hospitalizations may miss a critical window when earlier use could improve adherence, stabilize symptoms, and reduce healthcare utilization

Acknowledgments

The authors thank Colette Cunningham (ApotheCom, Yardley, PA) for assistance in the preparation of this poster, which was funded by Johnson & Johnson.

Disclosures

Dr Li reported receiving personal fees from SKB Consulting Inc and Cobbs Creek Healthcare, all unrelated to the submitted work. Ms Benson and Mr Bookhart reported being employees and stockholders of Johnson and Johnson. Dr Doshi reported receiving grants from Johnson & Johnson during the conduct of the study; personal fees from AbbVie, Acadia, Janssen, Merck, Otsuka, and Takeda; and grants from Merck and Spark Therapeutics unrelated to the submitted work. Dr Geng had no disclosures to report.

Presented at the American Society of Clinical Psychopharmacology (ASCP) Annual Meeting; May 26-29, 2026; Miami, Florida, USA

References

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. 5th ed. American Psychiatric Publishing, Inc.; 2013. 2. Marcus SC et al. *J Manag Care Spec Pharm*. 2015;21(9):754-768. 3. El Abdellati K et al. *Front Neurosci*. 2020;14:531763. 4. Olivares JM et al. *Ann Gen Psychiatry*. 2013;12(1):32. 5. Lin D et al. *CNS Drugs*. 2021;35(5):469-481. 6. Li P et al. *Adv Ther*. 2025;42(2):1251-1264. 7. Joo SW, Lee J. *J Clin Psychiatry*. 2026;87(1):25m16048.

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This study was funded by Johnson & Johnson.