

First-Generation Antipsychotic Shortages in the United States: Analysis of Utilization Patterns and Hospitalizations

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Background

- Treatment of patients with schizophrenia requires a tailored approach using antipsychotic medication to improve symptoms and prevent functional decline.¹
- Shortages of first-generation antipsychotic medications place patients in vulnerable scenarios if medication cannot be accessed, leaving prescribers to alter therapy without guarantee of a sustained response to the new treatment.²

Objective

To describe antipsychotic utilization patterns and inpatient hospitalizations following first-generation antipsychotic drug shortage or discontinuation.

Methods

Data source:

- 2016-2023 Komodo Healthcare Map
- Follow-up: One year after the shortage or discontinuation index date (i.e., initial shortage date listed by the US Food and Drug Administration).

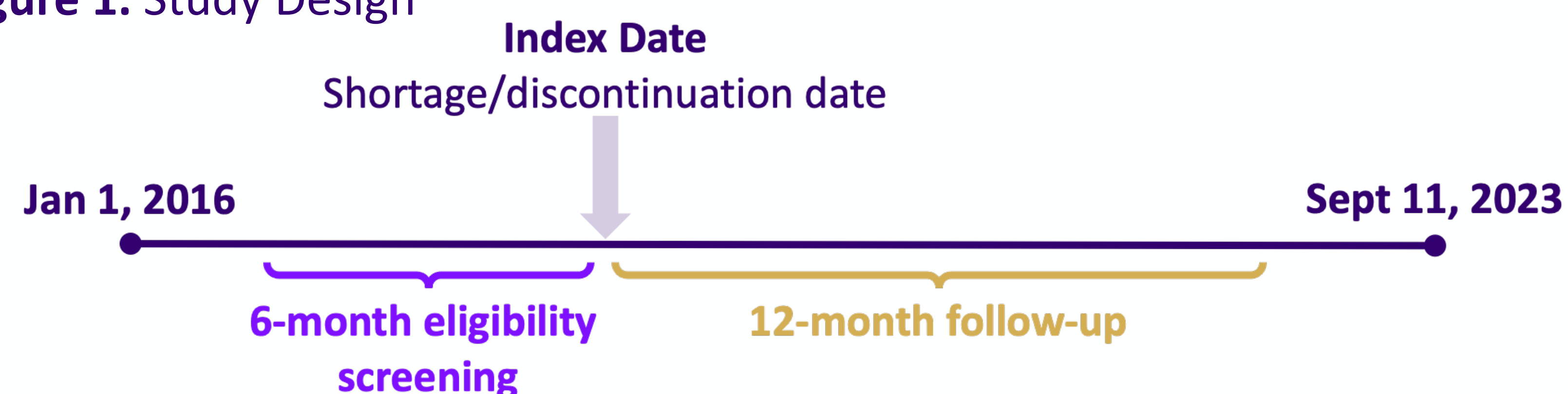
Study sample:

- Individuals with prescription claims for first-generation antipsychotics that were in shortage or were discontinued; fluphenazine, haloperidol, loxapine, molindone, perphenazine, pimozide, thioridazine, thiothixene, trifluoperazine.
- Six months of continuous treatment [medication possession ratio \geq 80%] and no inpatient psychiatric hospitalizations prior to the shortage or discontinuation index date, and at least one antipsychotic claim in the pre- and post-periods.

Outcomes:

- **Switching:** Proportion of individuals who switched to a different antipsychotic during the follow-up period.
- **Time to switch:** Number of days from index date to the first switch claim.
- **Number of switches:** Number of drugs among individuals who have switched.
- **Utilization:** Medications used post-shortage/discontinuation.

Figure 1. Study Design



Results

- Of the 150,608 individuals eligible for inclusion, 14,889 (9.9%) switched to a new antipsychotic medication during the follow-up period
- The most common switches post-index were to aripiprazole (11%), quetiapine (12%), and risperidone (16%).

Table 1. Demographic characteristics.

	Overall	Fluphenazine	Haloperidol	Loxapine	Molindone	Perphenazine	Pimozide	Thioridazine	Thiothixene	Trifluoperazine
N	150,608	18,863	82,795	5563	16	24,040	1880	5889	5631	5931
Age										
Mean (SD)	53.0 (15.7)	53.5 (14.2)	50.5 (15.4)	52.7 (14.7)	30.6 (14.7)	56.5 (15.9)	42 (20%)	61.3 (14.4)	58.8 (13.1)	61.7 (13.5)
Median	54.8	56.3	51.8	54.9	25.0	57.7	42.0	62.1	60.6	62.8
NA	1127 (0.01%)	100 (0.5%)	682 (0.8%)	25 (0.4%)	0 (0%)	168 (0.7%)	14 (0.7%)	49 (0.8%)	40 (0.7%)	50 (0.8%)
Sex										
Female	71,409 (47%)	8378 (44%)	35,970 (43%)	2884 (52%)	5 (31%)	14,201 (59%)	659 (35%)	2777 (47%)	3044 (54%)	3491 (59%)
Male	79,031 (53%)	10,464 (56%)	46,717 (56%)	2672 (48%)	11 (69%)	9826 (41%)	1219 (65%)	3104 (53%)	2584 (46%)	2434 (41%)
Unspecified	164 (0.1%)	20 (0.1%)	107 (0.1%)	7 (0.1%)	0 (0%)	12 (0.1%)	2 (0.1%)	8 (0.1%)	3 (0.1%)	5 (0.1%)
NA	4 (0%)	1 (0%)	1 (0%)	0 (0%)	0 (0%)	1 (0.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.0%)
RX Insurance										
Commercial	16,503 (11%)	1451 (8%)	6950 (8%)	731 (13%)	2 (13%)	4134 (17%)	796 (42%)	672 (11%)	866 (15%)	901 (15%)
Medicare	83,166 (55%)	11,381 (60%)	43,472 (53%)	3256 (59%)	6 (38%)	13,339 (56%)	596 (32%)	4086 (69%)	3477 (62%)	3553 (60%)
Medicaid	43,272 (29%)	5293 (28%)	28,011 (34%)	1366 (25%)	7 (44%)	5267 (22%)	386 (21%)	810 (14%)	990 (18%)	1142 (19%)
NA	7667 (5%)	738 (4%)	4362 (5%)	210 (4%)	1 (6%)	1300 (5%)	102 (5%)	321 (6%)	298 (5%)	355 (6%)

SD: standard deviation; RX: prescription drug

Table 2. Utilization and inpatient admissions.

	Fluphenazine	Haloperidol	Loxapine	Molindone	Perphenazine	Pimozide	Thioridazine	Thiothixene	Trifluoperazine
Switch, n (%)	1478 (8%)	7195 (9%)	581 (10%)	7 (44%)	1493 (6%)	77 (4%)	710 (12%)	1502 (27%)	1846 (31%)
Time to first switch, days	139 (99)	143 (95)	178 (115)	74 (72)	151 (98)	141 (90)	135 (71)	176 (81)	92 (70)
Switches, n (%)									
1	1224 (83%)	6129 (85%)	493 (85%)	6 (86%)	1257 (84%)	68 (88%)	586 (83%)	1133 (75%)	1405 (76%)
2	206 (14%)	885 (12%)	71 (12%)	1 (14%)	200 (13%)	6 (8%)	93 (13%)	277 (18%)	340 (18%)
3+	48 (3%)	181 (3%)	17 (3%)	0	36 (3%)	3 (4%)	31 (4%)	92 (6%)	101 (6%)
Patients w/ hosp., n (%)	1487 (8%)	5504 (7%)	216 (4%)	0	622 (3%)	6 (0.3%)	45 (0.8%)	206 (4%)	188 (3%)
Time to first hosp., Days	117 (117)	125 (120)	118 (124)	NA	138 (121)	84 (129)	150 (120)	179 (118)	168 (110)
Cost per admission, mean (SD)	\$2659 (2225)	\$2799 (2156)	\$1822 (1615)	NA	\$2032 (1542)	\$6086 (620)	\$2891 (921)	\$3319 (1585)	\$2944 (1749)

Conclusions

- ✓ Nearly one-third of patients receiving treatment with thiothixene (27%), trifluoperazine (31%), and molindone (44%) switched treatments after a shortage or discontinuation
- ✓ Switches were less common for medications with multiple suppliers and dosage forms
- ✓ Hospitalizations do not appear to be impacted
- ✓ Switch to a second-generation antipsychotic was more common

References

1. Keepers GA, Fochtman LJ, Anzia JM, Benjamin S, Lyness JM, Mojtabai R, et al. The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia. *Am J Psychiatry* 2020;177:868-72.
2. Levin, Saul. "The Impact of Stimulant Shortages on Patients: Cases from Members of the APA ." July 7, 2023. American Psychiatric Association, Washington, D.C., USA. <https://www.psychiatry.org/getattachment/3d0a8c7e-0f89-4f6c-ab56-5dd4f5c59f8b/APA-House-EC-Senate-Finance-RFI-Drug-Shortages-07072023.pdf>. April 1, 2024.